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A.M.A. ARCHIVES OF NEUROLOGY & PSYCHIATRY

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New Cover Design

With this issue, the A. M. A. Archives of Neurology and Psychiatry presents a new cover design and a slight modification of page format.

Two elements contribute to an attractive cover—simplicity and cleanliness. We believe that we have obtained the two primary objectives necessary in a cover design of this nature: namely, that it is attractive and that it conveys the subjective feeling of the unit which it represents, as well as legibility, which is important in this case because of the contents listing involved. This cover is fluid enough to attractively accommodate varying lengths of contents listing. By the use of a simple line or block treatment, and by placing the contents upon a white background, we gain the maximum contrast possible, therefore, greater legibility.

The use of the seal has several functions: Being a circle in design, it relieves to an extent the over-all use of lines, squares, and rectangles; it stands as a symbol for the many years of dedicated service by an organization of the American Medical Association's stature in the advancement of knowledge in specialized fields, thus adding immeasurably to the effectiveness of the design.

The change in page format is confined to the title, subtitle, and authors' names. The change from a Coronet Bold type face to Bodoni Bold will eliminate the difficulty encountered when reading a formula or an abbreviation in script capitals. The use of Antique Italic for subtitles and Spartan Bold for the authors creates a desirable distinction between these parts. The arrangement realizes a saving in space.

This new cover is a development of an idea. It is not the result of a sudden thought. First, a suggestion was presented which was nothing more than a different arrangement of familiar elements. Then followed the collection of reactions, suggestions, and additional experimentation in search for the inspiration. All of the separate bits of information gathered were thoroughly digested, and the relationship between elements was established. The result is the crystallization of the idea. In following this procedure, our readers and editors have contributed immeasurably to the end product. Their cooperation means a new design of lasting quality.

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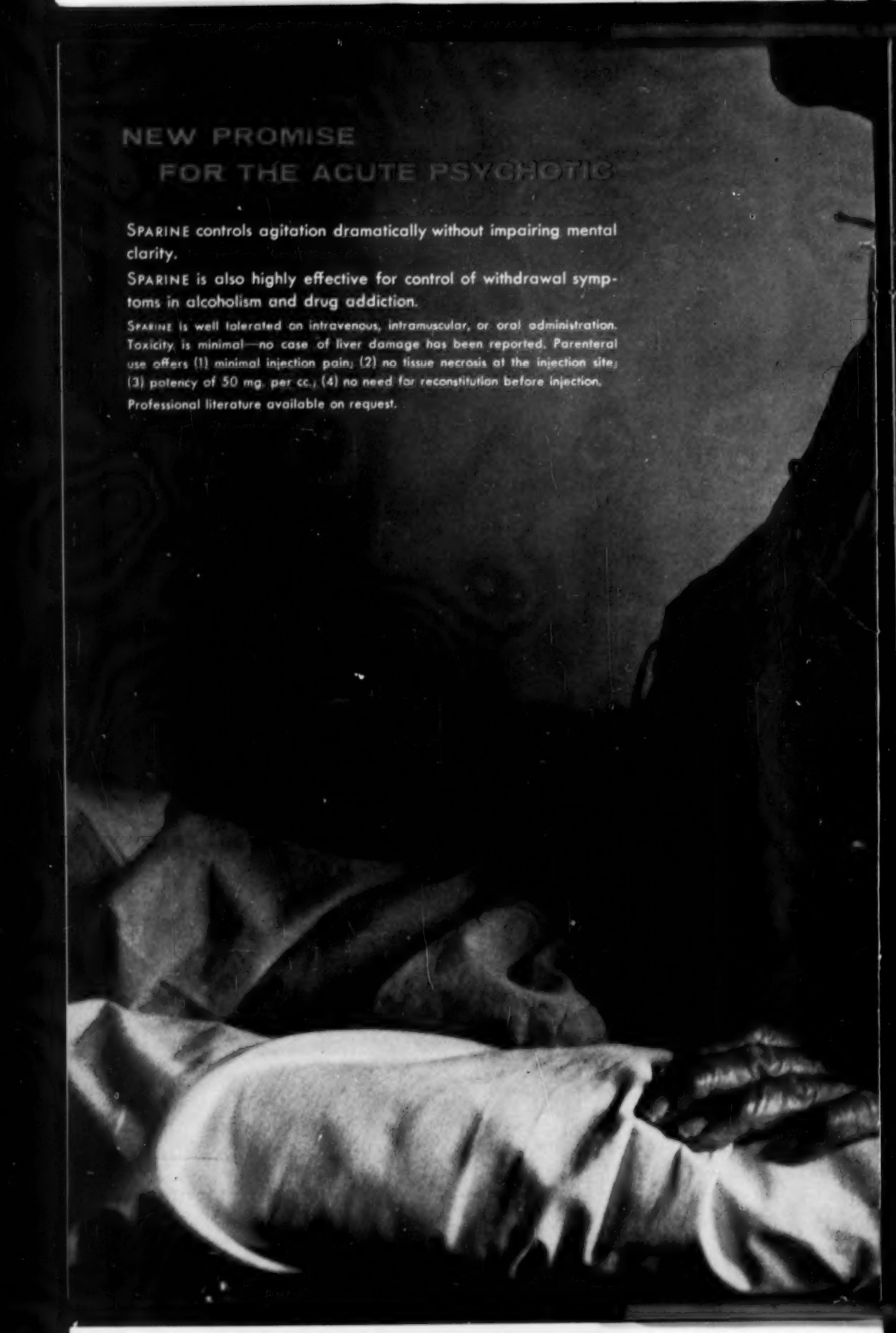
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Permanent Relief of Tic Douloureux by Gasserian Injection of Hot Water

RUDOLPH JAEGER, M.D., Philadelphia

A safe, effective method for injecting the Gasserian ganglion to stop permanently the atrocious face pain of tic douloureux and cancer has long seemed desirable to replace the time-tested but generally considered hazardous technique employing alcohol or other destructive chemical agents. Numerous attempts to control the sharp, stabbing, recurring agonizing pain so characteristic of tic douloureux have been made by using various drugs through their systemic effect; but those that have given some promise of producing permanent relief are not without the danger of causing serious permanent damage to the brain (stilbamidine[1,2] [4,4′-stilbenedicarboxamidine] and trichloroethylene[3-5] [$CHCl\text{-}CCl_2$]). Because of the spontaneous remissive nature of tic douloureux, it has been extremely difficult to evaluate accurately the relief, if any, produced by the many empirical treatments that have been tried. Those patients treated by nonspecific medical methods too frequently become discouraged, despondent, anxious persons who lose confidence in their attending physicians and medical science in general. They learn from numerous and varied experiences that the implied promised relief from their suffering by such therapies is not forthcoming and withdraw from society into a mental state of doubt and frustration and a dogged stoicism that is indeed remarkable.

The development of operative methods through craniectomy has led to satisfactory, specific, predictable relief from the pain of tic douloureux by the selective cutting or destruction of parts of the ganglion or its sensory root, under direct vision. However, such procedures require entering the brain cavity and exposing the patient to an operation of considerable magnitude with many potential hazards, which many of them are in poor condition to withstand. The majority of them are elderly and suffer from major metabolic disturbances and chronic crippling disorders, as well as from the ravages of arteriosclerosis of the brain, heart, and kidneys which preclude operative measures. Furthermore, all the operations as yet devised carry an appreciable risk of permanent paralysis of the face and the muscles of mastication, which has not been present in this group of 100 cases treated with hot water injected into the ganglion.

That alcohol or any other neurotoxic drug injected into the Gasserian ganglion, as proposed by Härtel,[6] will give permanent relief of trigeminal pain by chemically destroying the ganglionic cells is not to be questioned. This phenomenon is based on the fundamental anatomic fact that the sensory nerve cells

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From the Department of Neurological Surgery, Jefferson Medical College and Hospital and Wills Eye Hospital.

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and primary axons for the transmission of afferent stimuli from the face to the brain are in the Gasserian (trigeminal) ganglion. It has been observed and generally acknowledged that a destroyed nerve cell cannot be replaced. Therefore, its complete destruction by any agent produces a permanent loss of the function formerly performed by the cell. Harris,[7] in 1940, published his experience and extremely satisfactory results with this method in 1433 cases. However, its occasional devastating paralysis of the cranial nerves (3rd, 4th, 6th, 7th, 8th, 9th, 10th, and 11th) has deterred most surgeons from accepting this procedure as the one of choice. In recent questionnaires returned from 52 leading neurosurgeons of this country holding positions as chiefs of neurosurgery in prominent medical schools, only one voiced his approval of this method and advocates its use. The other 51 replying did not use ganglion injection of any type.

Injection of hot water into the Gasserian ganglion as a destructive agent was preceded by considerable investigation and experience with the injection of water of varying temperatures into the frontal lobes to produce regressive tranquilizing effect in the treatment of the pain and anxiety of cancer and the anxiety and emotional states in a variety of mental disturbances, (unpublished investigation now in progress). This entailed the making of burr openings through the skull over the frontal lobes and coagulating all of the cortical vessels on and just beneath them. It was possible to inject repeatedly elected locations of the brain through the openings on subsequent occasions and produce a lobotomy effect without the risk of massive hemorrhage and with complete control over the degree and progress of mental change. It was logical to conclude that if water at 75 to 100 C, which were the temperatures tested, could produce the observed regressive changes in the neural elements of the frontal lobe, then boiling water injected into the Gasserian ganglion should cause permanent destructive changes and loss of function in the ganglion cells. Wide diffusion of hot water, with injurious effects beyond the point of injection, seemed improbable, since, as it spreads through the cerebrospinal fluid, bathing the ganglion in Meckel's cavity, its temperature is immediately reduced to an innocuous point except very near the needle tip.

The first patient receiving injection demonstrated the efficacy of this method for producing a permanent crippling or destruction of the ganglion cells. This and subsequent injections have shown that the extent of the effect on the nerve cells, axones, and nerve fibers is in direct relation to the temperature and quantity of the water that bathes these neural elements.

On Sept. 4, 1953, a feeble 78-year-old woman, suffering from tic douloureux, who had been repeatedly relieved by peripheral-branch alcohol injections, was treated by injecting 1.5 cc. of boiling water into the ganglion through the foramen ovale under x-ray guidance. She had immediate hypalgesia over the entire side of the face. There has been no change of her sensory pattern, and she has been free of pain since. This experience has now been repeated many times with a similar postinjection effect.

Technique of Injecting the Gasserian Ganglion with Hot Water

The injection is performed in the neuroradiology room on a Franklin radiographic headstand under very light thiopental (Pentothal) sodium anesthesia. With a "twilight-sleep" depth of anesthesia one can determine during the injection, and with great precision, the extent and degree of analgesia or hypalgesia, by the involuntary muscular responses of the patient's face and feet to pinprick over the painful area, even though there is no apparent conscious knowledge on the patient's part of the painful stimuli which are applied. Insufficient hypalgesia or anesthesia over the affected part of the face may require repeating the injection or increasing the amount of boiling water.

A short beveled 3¼ in. 17- or 18-gauge spinal needle is inserted through the cheek below the malar bone and medial to the ramus of the lower jaw, making certain by direct intraoral inspection that the needle has not punctured the mucous membrane and contaminated the needle point. It is pointed to a location anterior to the foramen ovale at the base of the skull, where its tip is precisely located by the x-ray on Polaroid or conventional film taken from below the mandible on a line perpendicular to the base of the skull. By carefully maneuvering the needle tip toward and barely through the foramen ovale by repeated roentgenograms, one can be certain at all times of its depth and exact location. On visualizing and palpating the foraminal opening, the needle is advanced 1 cm. through it, where it will lie very near or among the ganglion cells. Cerebrospinal fluid may be obtained, but this is unnecessary for obtaining a good result. If fluid should be obtained, not more than 0.5 cc. of boiling water is injected as the initial amount, although by successively increasing this by 0.5 cc. each time, it may require as much as 2 cc. at a single injection to produce the desired result. After each individual injection its effect is determined by the patient's reaction to pinprick stimulation of the face. Hypalgesia of the painful area is apparently all that is required to stop pain in most instances. If the fluid-bearing subarachnoid space around the ganglion has not been entered, slightly larger amounts of water will usually be necessary, but more than 2.5 cc. at a single injection has been considered unwise for fear of causing a temporary paresis of the extraocular nerves. In the event of a failure it is better to wait for two days and then repeat the procedure.

Summary of Cases Treated

One hundred patients with typical tic douloureux (major trigeminal tic) have had ganglion injections with boiling water (actually 80 C at the needle point in the ganglion) by the method described. There were five with immediate recurrence of their pain, which was relieved by suboccipital craniectomy and partial posterior root section. One of these, on whom a classical partial root section was done, had a recurrence of the pain a year later in the unanesthetized facial area, which was successfully and easily relieved by total ganglion destruction by injecting 0.75 cc. of boiling water. Each of these failures had venous bleeding at the foramen ovale which cooled the water injected to an ineffective temperature, so that only a moderate hypalgesia resulted. By greater experience and improvement in technique this cause for failure should be rare. Actually, there has been only one failure in the last 70 patients treated. This woman was successfully relieved three weeks later.

Complications Following the Procedure

Of the 100 patients injected there was not one with facial paralysis or weakness. Lacrimation was occasionally temporarily reduced, but in no instance was there indication of tearing being absent. In all patients the cornea appeared normally moist after a few months. The greater deep petrosal nerve, which activates the lacrimal secretions, lies just beneath the trigeminal ganglion. If the elements of this nerve are not disturbed by the injection, then there is no temporary dryness of the eye. Should the parasympathetic fibers be paralyzed, then temporary dryness of the eye will occur, but there is a restoration of normal lacrimation when these fibers regenerate. For this reason there have been no late eye complications, and very few should be expected. Often it was noticed that the conjunctiva was slightly irritated immediately after the injection. This apparently was a part of facial swelling from needle puncture trauma. In one patient there was a slightly congested conjunctiva associated with a tiny corneal abrasion, which persisted only four days. Corneal sensation remained intact in most of the patients, since it was seldom necessary to produce complete facial anesthesia

Figs. 1-8.—Sample group of sensory patterns following injection of the ganglion with boiling water for tic douloureux. The areas of hatchure represent anesthesia; the stippled areas, hypalgesia. Fig. 1.—Tic douloureux of left upper jaw and lip. Fig. 2.—Pain in upper lip only. Fig. 3.—Pain in right lower jaw, lip, and tongue. Fig. 4.—Pain in right upper jaw and lip.

Fig. 5.—Pain in right upper jaw and lip. Fig. 6.—Pain primarily in left lower jaw and lip with some pain in upper lip. Fig. 7.—Pain in left lower jaw and lip. Fig. 8.—Pain over entire right side of face.

to stop the pain. Hypalgesia over the area affected by the pain appears to be adequate to stop it, and complete anesthesia of the region has seldom been sought for. Actually there has been little or no complaint from those patients with complete half-face anesthesia from massive ganglion cell destruction, nor has there been a late corneal or visual disturbance. The same lack of discomfort has been noted in total sensory root section by the suboccipital approach in a recent review of a group on whom that operation was performed.

The muscles of mastication have been partially or completely paralyzed in every patient. Full chewing strength returned in three or four months from regrowth of the motor branch because it is composed entirely of peripheral nerve fibers.

Two early patients had stuffiness of the ear, which disappeared in a matter of several months. This probably was caused from hemorrhage near the Eustachean tube, produced by the needle puncture. Occasionally a hematoma causes swelling and discoloration of the face and neck, which lasts a week or two.

Diplopia occurred temporarily in five patients from slight weakness of the third, fourth, or sixth cranial nerve. This probably is the result of the heat extending to these nerves where they lie very near the ganglion, when the quantity of water has been too large. This has always disappeared in from three to five months when these nerves have regenerated. This temporary complication has become very rare with additional experience.

Herpes often occurs after operative procedures and alcohol injection. In two patients of this group there were several small blebs on the lower lip. In a number of patients there was a small ulcer—undoubtedly herpetic in origin—on the mucous membrane of the lower lip. These all healed in less than three weeks. Two patients had some headache and what appeared to be a mild meningeal reaction. One had herpes on the upper and lower lips and eyelids. No complication resulted from this, and it was thought to have been caused by an excessive amount of boiling water that had been injected. One of them had a large herpetic eruption over the upper and lower lips on the side opposite that of the injection. Apparently the meningismus, which lasted only 24 hours, was due to the activation of intracranial herpetic virus.

*Results of Hot Water Injection in Tic Douloureux**

Result	No. of Patients
Completely relieved of sharp tic pains	93
No relief (relieved by operation)	4
Partial but satisfactory relief (some twinges present, but not distressing)	3
Reinjection (many months later) because of extension of pain to area not previously involved	2
Facial paralysis or weakness	None
Corneal ulcer or corneal complications	None
Facial herpes	3
Extraocular weakness (lasting from 3-5 mo.)	5
Serious complications	None
Deaths or postinjection shock	None
Severe postinjection paresthesias (only one of these preferred the tic pain to the paresthesia)	4

* First 100 patients.

Conclusion

The procedure of Gasserian ganglion cell destruction by injecting boiling water into this nerve center has been effective in safely stopping the pain of tic douloureux in 96 out of 100 patients. Two, with inadequate facial hypalgesia, had a late return of pain, which was stopped by a second injection.

To date, it appears that this method is as permanent a cure for tic douloureux as is available at the present time, although it must be acknowledged that any treatment that does not destroy every single ganglion cell or every sensory root fiber back of the ganglion may fail, because pain may return if the disorder should extend to those parts of the face not completely anesthetized. However, should the pain extend to other parts of the face not formerly affected, another injection can be performed with no greater risk or pain than the first one. The advantage of this method appears to be the avoidance of a major brain operation with its shock, low mortality, permanence, absence of serious eye complications, no facial paralysis, and painlessness.

This procedure is not recommended for those untrained in detailed intracranial anatomy. Its technical aspects require the knowledge and experience equivalent to that of a neurosurgeon for safe and satisfactory results.

Jefferson Hospital.

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Brain Copper-Protein Fractions in the Normal and in Wilson's Disease

HUNTINGTON PORTER, M.D., and JORDI FOLCH, M.D., Boston

Alteration in copper metabolism is well established as a consistent feature of hepatolenticular degeneration (Wilson's disease). A number of different aspects of this metabolic abnormality have been described. The copper content of brain, liver, and other organs is increased.* Urinary excretion of copper is increased,† but fecal excretion is decreased,‡ the patients showing a positive dietary balance with respect to copper. Total serum copper is usually decreased,§ due to a marked reduction in ceruloplasmin,‖ whereas the amount of plasma copper loosely bound to protein and reacting directly with sodium diethyldithiocarbamate is increased.[4] Studies with radioactive copper have indicated increased absorption of copper from the gastrointestinal tract ¶ and demonstrated relative persistence of administered copper in the albumin fraction of serum, as opposed to the transfer into the ceruloplasmin-containing globulin fraction which occurs in normal persons.# Improvement in neurological symptoms in some cases following administration of dimercaprol U. S. P. (BAL), noted by several observers,* has suggested that the neurological manifestations of this disease may be related to the accumulation of copper in the brain.

Previous preliminary communications † have described the development of procedures for the separation of brain tissue components into three different copper-containing fractions and for the isolation, from one of them, of a protein subfraction containing 0.14% copper. The further purification of this subfraction to yield a green copper protein, which is homogeneous on paper electrophoresis, will be reported elsewhere.‡ To our knowledge, no other data have been available on the condition in which copper is present in either normal or pathological brain. The present paper describes the application of the above fractionation procedures to brains with hepatolenticular degeneration and reports in more detail the results from normal human and bovine brain.

Material and Methods

The normal human brains used in the fractionation procedure were from patients dying abruptly of such causes as myocardial infarction, pulmonary embolus, and dissecting aortic aneurysm. The three brains studied as examples of hepatolenticular degeneration were from well-established cases of this disease with Kayser-Fleischer rings. Descriptions of clinical aspects of these cases are available in other papers.§ The normal brains were taken directly into glass containers at the time of autopsy. The portions of brain from nepato-

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† References 5, 6.
‡ References 4, 7.
§ References 8, 9.
‖ References 10, 11.
¶ References 12, 13.
# References 14, 15.

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† References 19, 20.
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lenticular degeneration Cases 1 and 2‖ were also collected without contact with metal at the time of autopsy. The material from Case 3¶ had also been protected from contamination with extraneous copper and was received wrapped in Parafilm and frozen in carbon dioxide snow (dry ice).

The meninges were stripped from each brain under cold redistilled water. Thereafter all fractionation procedures were carried out in a cold room at 4 C. Gray matter was obtained by scraping cerebral cortex from the chilled brain with a wooden tongue depressor. White matter was obtained by dissecting out the corpus callosum and centrum semiovale with a glass knife. The tissue was homogenized by freezing at −10 C, followed by partial thawing and grinding in a mortar with 90-mesh Alundum (electrically fused aluminum oxide). Scrupulous precautions to avoid contamination with extraneous copper were taken throughout the fractionation procedures and analyses. All glassware was cleaned by allowing it to stand overnight in 6 N HCl prior to each use, followed by exhaustive rinsing, and the Alundum used in grinding the tissue was similarly cleaned with the addition of an initial two-hour period in contact with boiling 6 N HCl. All water used was redistilled over glass. The acetate buffer, which, when made from reagent-grade chemicals, contained appreciable copper, was made copper-free by the addition to each liter of buffer of 1 cc. of a 2% solution of sodium diethyldithiocarbamate, followed by extraction four times with 10 cc. portions of carbon tetrachloride. In order to confirm that the conditions employed were, in fact, not introducing extraneous copper, the grinding and tissue extraction procedure was carried out in quadruplicate as a blank without tissue but using Alundum and acetate buffer, both freed of extraneous copper as above. It was demonstrated that the grinding and tissue extraction procedure would not contribute more than 0.07γ of copper per gram of fresh tissue, which would amount to less than 3% of the copper in bovine cortex. Copper determinations were carried out in duplicate by the method of Eden and Green,[21] modified as previously reported.[8]

‖ Made available through the courtesy of Dr. D. Denny-Brown and Dr. J. M. Foley.

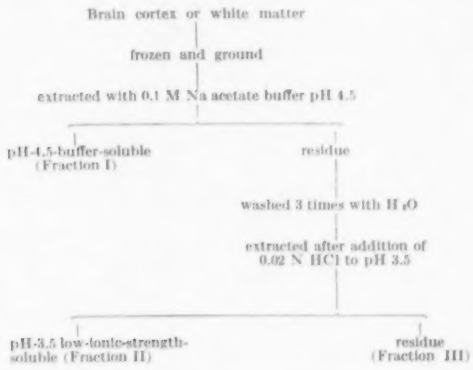
¶ Made available through the courtesy of Dr. G. E. Cartwright.

Results

Procedure for Separation of Brain Proteins into Three Copper-Containing Fractions

Table 1 outlines in schematic form the procedure which was developed for separation of brain proteins into three different copper-containing fractions. To the homogenized fresh tissue was added 0.1 M sodium acetate buffer pH 4.5 in the proportion of 2 cc. per gram of fresh tissue, and the mixture was stirred for one hour using a glass stirrer. After centrifugation of the mixture for 45 minutes at 2600 g, a clear brownish-red supernatant could be decanted (Fraction I). In calculating yields of copper and protein, the water contributed by the tissue to the final buffer volumes was computed as 0.85 cc. per gram of fresh tissue for cortex and as 0.70 cc. per gram of fresh tissue

TABLE 1.—*Procedure for Separation of Brain Copper-Protein Fractions*


Brain cortex or white matter
frozen and ground
extracted with 0.1 M Na acetate buffer pH 4.5
pH-4.5-buffer-soluble (Fraction I)
residue
washed 3 times with H_2O
extracted after addition of 0.02 N HCl to pH 3.5
pH-3.5 low-ionic-strength-soluble (Fraction II)
residue (Fraction III)

for white matter. The buffer-insoluble tissue residue was then washed by addition of 4 cc. of water for each gram of starting fresh tissue, followed by thorough mixing, centrifugation, and decantation of the clear supernatant that had separated. The washing with water was repeated two or three times, with resulting reduction in the ionic strength of the solution wetting the tissue residue to less than 0.001. To the washed residue, 0.02 NHCl was then slowly added dropwise with mechanical stirring, using a glass stirrer, until the suspension reached a pH of approximately 3.5. To bring the suspension to this pH required about 2.5 cc. of 0.02 N HCl per gram of starting fresh tissue, making the final aqueous volume about 3 cc. per gram of fresh tissue. The mixture was stirred for 30 minutes and then centrifuged for 2 hours at 2600 g. Even after this long a period of centrifugation, the sediment remained poorly packed, but it was possible to decant or siphon off a faintly brownish, opalescent supernatant (Fraction II). The pH 3.5 insoluble residue (Fraction III) could be freed of the remaining pH 3.5 soluble material by washing repeatedly with water, followed by washing with acetone prior to drying.

In the case of bovine brain, it was found that water extracts # and 0.1 M sodium bicarbonate buffer extracts pH 8.2 of the tissue contained amounts of copper similar to those present in pH 4.5 acetate buffer extracts (Fraction I). It was established that the same copper fraction was present in the three different extracts by extracting the tissue, on the one hand, with acetate buffer and then with bicarbonate buffer, and, on the other hand, with water and then with acetate buffer. In both cases it was found that the second extract contained only that amount of copper which could be accounted for by the portion of original extract remaining with the tissue residue after the first extraction. Water or bicarbonate buffer extractions, however, yielded the Fraction I copper-protein in a less concentrated form, since they extracted larger amounts of other proteins than did the pH 4.5 acetate buffer.

Distribution of Copper Between the Three Fractions in Bovine Brain

The fractionation procedure outlined above was developed with bovine brain. The relative amounts of tissue copper extracted in each of the first two fractions, as obtained from six different preparations of bovine brain, are shown in the upper portion of Table 2. It is apparent that both Fraction I and Fraction II were quite consistent in yield of copper and of total solids as measured by dry weight. In the case of Fraction I, the solids were determined after dialysis to remove the acid-soluble components of low molecular weight. The solids from Fraction I and Fraction II contained from 12.3% to 14.5% nitrogen, indicating that they were mainly protein. Both fractions from bovine cortex were also exhaustible. Thus, washing the tissue residue after the extraction of Fraction I with fresh buffer or washing the tissue residue after the extraction of Fraction II with water, maintaining the pH at 3.5, failed in both cases to extract copper or nitrogen in excess of the amounts accounted for by the portion of original extract remaining in the residue.

The copper in both fractions was essentially undialyzable, even when dialysis was begun with the contents of the bag at the relatively low pH's used in the extraction procedures. In the case of Fraction II, more than one-third of the solids and of the nitrogen were found to be dialyzable. The fact that the tissue residue had been exhaustively washed with water prior to extraction of this fraction made it most unlikely that the dialyzable material represented residual acid-soluble components. This unexpected observation is being investigated further. That the major part of the copper in Fraction II was not attached to this dialyzable material was further dem-

In order to obtain clear water extracts, it was necessary to centrifuge at 44,000g. Centrifugation at 2600g yielded only gross suspensions, which may contain the major portion of tissue components.

onstrated by analysis of the external solutions, the copper content of which ranged only from zero to 21% of the initial Fraction II copper. Moreover, proteins containing more than 80% of the copper in this fraction could be precipitated by raising the pH to 5.5.

As can be seen from Table 2, the sum of the copper extracted in Fraction I plus that in Fraction II did not account for the total fresh tissue copper. By subtracting the sum of the copper in the first two fractions from the total tissue copper, about one-third of the total copper in both bovine cortex and bovine white matter could be assigned to residual fraction III. That this residual fraction really contains copper, and is not a computation artifact, was shown by copper analyses on such residues from three different preparations of bovine cortex. They were found to contain, respectively, 0.59γ, 0.82γ, and 1.22γ of copper per gram of fresh tissue. In these three preparations, the sum total of copper in Fractions I, II, and III amounted to from 98% to 114% of the total fresh tissue copper.

Distribution of Copper Among the Three Fractions in Normal Human Brain

The fractionation procedure was also applied to four normal human brains, with the results shown in Table 2. Comparison of the human values with those obtained from bovine brain reveals some noteworthy differences between the two species with

TABLE 2—*Copper and Solids Extracted in Fractions I and II from Bovine Brain, Normal Human Brain, and Brains with Hepatolenticular Degeneration* *

Tissue		Total Tissue Copper	Fraction I Extracted by pH 4.5 0.1 M Acetate Buffer		Fraction II Extracted at pH 3.5 & Low Ionic Strength	
			Copper	Solids†	Copper	Solids †
Bovine cortex	A	2.58	0.91	6.28		
	B	2.00	0.73	6.04	0.60	31.4
	C	2.30	0.86	6.18	0.79	32.8
	D	2.85	0.99		0.84	36.7
	E	2.47	0.96		0.64	33.6
	F	2.59	1.01		0.68	31.6
	Mean	2.47	0.91 (37%)	6.17	0.71 (29%)	33.2
Bovine white matter	A	1.03	0.51	3.67		
	B	0.97	0.38	2.43		
	C	1.05	0.51	3.19		
	D	0.94	0.51		0.13	12.8
	E	0.98	0.52		0.19	12.9
	F	1.05	0.54		0.15	9.0
	Mean	1.00	0.50 (50%)	3.10	0.16 (16%)	11.6
Normal human cortex	A	4.00	2.44	6.81		
	B	4.47	2.62	7.04	0.97	32.4
	C	3.45	2.29	7.72	0.84	28.3
	D	4.12	2.72		0.92	28.3
	Mean	4.01	2.52 (63%)	7.19	0.91 (23%)	29.7
Normal human white matter	A	4.33	2.28	4.62		
	B	4.81	2.95	5.39	0.46	15.3
	C	2.72	1.90	3.12	0.38	14.4
	D	4.74	2.89		0.45	14.8
	Mean	4.15	2.51 (61%)	4.38	0.43 (10%)	14.8
Hepatolenticular degeneration cortex	1	60.8	44.2 (73%)			
	2	56.5	46.0 (85%)	7.07	5.98 (11%)	28.6
	3	61.3	41.5 (68%)	5.14	7.34 (12%)	10.1

* Copper expressed as micrograms per gram of fresh tissue. Solids expressed as milligrams per gram of fresh tissue. Percentile values, in parenthesis, refer to the proportion of total fresh tissue copper obtained in each fraction.

† Determined after dialysis.

respect both to the total tissue copper and to the distribution of copper among the three fractions. First, it can be seen that both human cortex and human white matter contain substantially larger amounts of total tissue copper than their bovine counterparts, and that, in this study, the average total copper content of human white matter approximated, and indeed slightly exceeded, the total copper content of human cortex. Second, a greater proportion of the total tissue copper of human brain was extractable in Fraction I, this fraction accounting for more than 60% of the total copper in both human cortex and human white matter. A correspondingly smaller proportion of total tissue copper could be assigned to Fraction III of human cortex, whereas the proportions of the total tissue copper obtained in Fraction II from human cortex and from human white matter were only slightly less than the corresponding bovine values. The copper content of human Fractions I and II, like that of their bovine counterparts, remained undiminished by dialysis, and proteins containing approximately 80% of the copper in human Fraction II could be precipitated by raising the pH to 5.5. Solids in human Fractions I and II also contained about 14% nitrogen.

Fractionation of the Pathological Copper in Brains from Cases of Hepatolenticular Degeneration

The results obtained by applying the fractionation procedure to cerebral cortex from three cases of hepatolenticular degeneration are shown at the bottom of Table 2. In these three brains, with a total cortex copper content increased to between 13 and 15 times the normal average, copper extracted in Fraction I accounted for from 68% to 85% of the total. Yields of total solids, particularly those extracted in Fraction II, were diminished in Case 3. In Case 2, however, the yields of protein were similar to the normal values, and it is possible that the low figures in Case 3 represent a postmortem artifact. At the time the material from Case 1 was received, only the acetate buffer extraction step had been developed. Cortex from the other two cases, however, was put through the entire fractionation procedure, including analyses of the washed residual Fraction III. In Case 2, Fraction III contained 3.28γ of copper per gram of fresh tissue, or 6.1% of the total fresh tissue copper. In Case 3, Fraction III contained 6.14γ of copper per gram of fresh tissue, or 10% of the total fresh tissue copper. Thus, all three fractions contributed, although in varying degree, to the abnormal increase in brain copper in hepatolenticular degeneration. The sum of the copper recovered in each of the three fractions individually amounted to 102% of the total fresh tissue copper in Case 2 and to 90% of the total fresh tissue copper in Case 3.

Dialysis of the pH 4.5 buffer extracts containing Fraction I against water resulted in a marked loss of copper in the two pathological brains in which it was carried out, as opposed to normal brains, in which none of the Fraction I copper was dialyzable. In Cases 2 and 3, respectively, the dialyzed extracts retained 26.8γ and 21.9γ of copper per gram of fresh tissue, or 58% and 53% of the starting Fraction I copper. This loss of copper on dialysis might have resulted either from a copper-protein linkage unstable at pH 4.5 or from a combination of some of the copper with dialyzable components of small molecular weight. The identity in bovine cortex of the copper extracted by 0.1 M sodium bicarbonate buffer pH 8.2 with that extracted as Fraction I by pH 4.5 acetate buffer seemed to offer a means of determining which of these possible mechanisms was operating. Since dialysis of bicarbonate buffer extracts against water resulted in the formation of a considerable precipitate, the bicarbonate buffer extracts were instead dialyzed against 0.1 M bicarbonate solution. For this purpose, preparations of cortex from Cases 2 and 3 each were extracted with four volumes of 0.1 M sodium bicarbonate. The copper

extracted amounted to 45.1γ per gram of fresh tissue in Case 2 and 46.9γ per gram of fresh tissue in Case 3, or 98% and 113%, respectively, of the copper extracted by the pH 4.5 acetate buffer. Duplicate aliquots of the bicarbonate buffer extracts from each case were then dialyzed over three successive 48-hour periods against three successive portions of ninefold their volume of bicarbonate buffer. Copper retained after dialysis amounted in the duplicate experiments to 107% and 112% of the initial bicarbonate buffer extract copper in Case 2 and to 100% and 95% of the initial bicarbonate buffer extract copper in Case 3. That significant quantities of copper were not lost on dialysis against bicarbonate buffer was further verified by analyses of the first external solutions, which contained zero and 9% of the initial bicarbonate buffer extract copper in Case 2 and 1% and 10% of the initial bicarbonate buffer extract copper in Case 3. It was therefore concluded that the copper loss on dialysis of the original pH 4.5 buffer extracts was the result of instability of the copper-protein linkage to this pH, and that substantially all of the pathological copper in the brain in hepatolenticular degeneration is bound in undialyzable form, presumably to proteins. These results also indicated that in hepatolenticular degeneration a considerable portion of the pathological copper is present in a form that is different from any occurring in appreciable amounts in normal brain. This abnormal copper-protein combination is characterized by solubility in pH 4.5 acetate buffer and also in pH 8.2 bicarbonate buffer, and by loss of copper on dialysis at pH 4.5, but by retention of copper on dialysis at pH 8.2. If the copper extracted from these pathological brains by bicarbonate buffer is strictly identical with that extracted by acetate buffer, as can be shown for bovine brain, the copper in this abnormal form might be equivalent to the copper lost on dialysis of the pH 4.5 buffer extract, that is, about one-third of the total fresh tissue copper.

Comment

Early in the course of this investigation, it was found that, in bovine brain, total lipid extracts,[22] including proteolipids,[23] contained no copper. The problem of the types of organic combination in which copper is present in brain therefore became part of the larger problem of development of procedures for the extraction and isolation of brain proteins in general. Equal quantities of copper were obtained by extracting the fresh tissue with 0.1 M acetate buffer at pH 4.5, with water alone, or with 0.1 M sodium bicarbonate at pH 8.2, and the identity of the copper extracted could be demonstrated by successive extractions with the different mediums in varying order. Of these three alternative procedures, extraction with acetate buffer had two distinct advantages over the other two mediums as an initial step in the separation of brain copper-proteins. First, clear separation of supernatant and sediment was readily obtained on centrifugation at relatively low g values, thus obviating the need for more elaborate centrifuging equipment, which was both less suitable for large-scale preparations and more likely to introduce contamination with extraneous copper. Second, between 37% (bovine cortex) and 63% (human cortex) of the total fresh tissue copper could be concentrated in a fraction containing not more than 7% of the total brain proteins, whereas both water and bicarbonate buffer extracted additional amounts of unrelated copper-free proteins. The acetate buffer extracts were also consistent in yield of copper and of solids, and were exhaustible, repetition of the extraction of the tissue residue with fresh buffer yielding no additional copper or protein. A possible disadvantage of the extraction with acetate buffer was the possibility of loss of copper from the naturally occurring copper-protein at pH 4.5, since certain purified copper-proteins, for example, ceruloplasmin,[24] have been reported to lose copper at this pH. The pH 4.5 acetate buffer extracts of brain, however, lost no copper even on prolonged dialysis

against acetate buffer at the same pH. Extraction of the fresh tissue with 0.1 M acetate buffer pH 4.5 was therefore adopted as the routine initial step in the separation of brain copper-proteins, and the copper-proteins so obtained are designated as Fraction I. Both the stability of the copper in this fraction to dialysis at pH 4.5 and the extractability of the same copper-containing fraction over a pH range of 4.5 to 8.2 strengthen the likelihood that the copper-protein so obtained is not an artificial product of the procedure of preparation, but is a naturally occurring copper-protein.

A second copper-containing protein fraction, designated Fraction II, could be extracted from the residue of Fraction I by lowering the pH to 3.5 and the ionic strength to less than 0.001. That lowering both pH and ionic strength might lead to extraction of another group of brain proteins was not unexpected in view of the general observations of a class of proteins "in which increase of ionic strength actually decreases solubility on the acid side of the isoelectric point."[25] This fraction, like Fraction I, was reproducible and exhaustible in yield of both copper and solids and retained its copper on dialysis. In the two species examined, the quantities of both copper and solids extracted as Fraction II from gray matter were at least twofold those extracted from white matter. The sum of the copper extracted in Fraction I plus Fraction II failed to account for the total fresh tissue copper in all four tissues examined, i. e., bovine cortex, bovine white matter, human cortex, and human white matter. The copper which could therefore be assigned to residual Fraction III amounted to about one-third of the total fresh tissue copper in all of the tissues examined except human cortex. For bovine cortex, the presence of copper in Fraction III was demonstrated by direct analysis of the washed residue, with recovery in the sum of the three fractions of 98% to 114% of the total fresh tissue copper.

In the brains from cases of hepatolenticular degeneration, all three fractions could be shown to contribute to the greatly increased total copper content. By far the greatest absolute amount of pathological copper, however, could be extracted in Fraction I. When the pH 4.5 acetate buffer extract containing Fraction I was dialyzed, it became apparent that, in hepatolenticular degeneration, the copper in this fraction existed in two different types of organic combination, one of which rendered the copper dialyzable at pH 4.5. This dialyzable copper might have represented either an instability of a copper-protein linkage to pH 4.5 or a primary combination of copper with nonprotein components of small molecular weight. The latter possibility required special consideration in view of the suggestion by Uzman[26] that the fixation of copper in organs like liver and brain may be due to the formation of copper-peptide complexes in the tissues. As in the case of bovine cortex, extraction of the fresh tissue from these pathological brains with pH 8.2 sodium bicarbonate buffer yielded amounts of copper similar to those obtained with the pH 4.5 acetate buffer. Dialysis of bicarbonate buffer extracts against bicarbonate buffer was carried out to determine whether significant quantities of copper were, in fact, bound to smaller molecules, such as peptides. Under these conditions no copper was dialyzable. It is concluded that substantially all of the copper accumulating in the brain in hepatolenticular degeneration is bound in undialyzable form, presumably to proteins. These results also indicate that in hepatolenticular degeneration a considerable proportion of the pathological copper, probably amounting to at least one-third of the total, is in a type of copper-protein combination not found in appreciable amounts in normal brain. This abnormal copper-protein is similar to normal Fraction I in being soluble both in pH 4.5 acetate buffer and in pH 8.2 bicarbonate buffer, but is different from normal Fraction I copper-protein(s) in its failure to retain copper on dialysis at pH

4.5. Since ceruloplasmin, for example, has been reported to lose only part of its blue color, or copper, at pH 4.5,* it may be that the proportion of the total tissue copper in this abnormal form is, in fact, considerably greater than the values indicated by the amount of copper actually lost on dialysis at this pH. It is possible that this abnormal type of copper-protein combination is related to the development of the neurological manifestations of this disease, perhaps by combining with, and inhibiting the enzymatic activity of, some normally copper-free protein(s). Since, of the brain copper-protein combinations studied thus far, this one appears to have the least firm copper-protein linkage, it is possible that it is this copper which is affected by treatment with dimercaprol. At the present time, there is no evidence as to whether the pH-4.5-dialysis-stable copper, amounting to one-third or more of the total fresh tissue copper, is or is not identical with the Fraction I copper of normal brain.

Summary

Brain proteins in hepatolenticular degeneration, like those in normal brain, can be separated into three copper-containing fractions: Fraction I, extracted with 0.1 M acetate buffer pH 4.5 (or with water or with 0.1 M bicarbonate buffer pH 8.2); Fraction II, extracted at pH 3.5 and vanishing ionic strength, and the residual Fraction III.

The greatest absolute amount of pathological brain copper in hepatolenticular degeneration is extracted in Fraction I. Of this Fraction I copper, slightly more than one-half is nondialyzable at pH 4.5 and may or may not be identical with the Fraction I copper of normal brain.

A significant portion of the pathological copper in the brain in hepatolenticular degeneration is present in a form not found in appreciable amounts in normal brain. This abnormal copper-protein combination is similar to normal Fraction I in being soluble both in 0.1 M acetate buffer pH 4.5 and in 0.1 M bicarbonate buffer pH 8.2, but is different from normal Fraction I copper-protein(s) in its failure to retain copper on dialysis at pH 4.5.

The finding that bicarbonate buffer extracts of the fresh tissue do not lose copper on dialysis against bicarbonate buffer indicates that substantially all of the copper in the brain in hepatolenticular degeneration is bound in undialyzable form, presumably to proteins.

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Incidence of Neurological Complications in Congenital Heart Disease

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Introduction

In the last few years there have been several papers on the association of cerebral abscess and cyanotic congenital heart disease.* Defects of the cardiac septum are a well-recognized feature of mongolism.[7] However, little or no emphasis has been placed on episodic loss of consciousness, convulsions, cerebrovascular accidents, and other neurological conditions. These are surprisingly common. It is the purpose of this paper to review the relative frequency of certain neurological complications of congenital heart disease as seen in the cardiac clinic of the Harriet Lane Home.

Material

Records of 1875 patients of the cardiac clinic at the Harriet Lane Home, The Johns Hopkins Hospital, were reviewed, covering the period from 1944 to 1955. Neurological complications following catheterization studies or operative intervention were not included. All diagnosed forms of malformations were included. However, such common types as patent ductus arteriosus and isolated septal defects were found to have very few neurological complications. Therefore, only a statistically significant sampling of these malformations was made. A few highly unusual malformations were not considered because information was too scanty to be of any statistical value. Percentages are given only where they are statistically significant.

The cardiac diagnosis was made mainly on clinical grounds, often verified by angiography, catheterization, or postmortem studies. The diagnoses were grouped according to basic types of cardiac defects. Group I is characterized by decreased pulmonary flow. In Group II transposition of the great vessels is most important. Group III includes malformations with essentially normal pulmonary circulation in early life. Group IV contains those cases with increased pulmonary circulation. Group V consists of septal defects and a patent ductus arteriosus, which are the so-called acyanotic forms of congenital heart disease.

In postmortem studies the clinical diagnosis was verified in about 90% of the cases of tetralogy of Fallot and transposition, in 50%-60% in which the diagnosis of single ventricle and tricuspid atresia was made, and in 60%-80% of the rest. Diagnostic errors between groups were rare.

A total of 481 patients, or 25.4%, had signs or symptoms of neurological disability.

Neurological Complications

I. Loss of Consciousness and Convulsions

Exclusive of convulsions, episodic loss of consciousness was noted in 225 patients. This resulted from severe cyanotic and dyspneic attacks, which are quite common in cyanotic heart disease. The period of unconsciousness lasted from minutes to two or three hours, and in some cases death followed. These episodes were characteristically brought on by exertion, feeding, bowel movement, etc., and were more frequently seen from the second half of the first year of life through 2 or 3 years of age. In many cases they recurred in less severe form for many years. Infrequently they would recur, or increase in severity, at the time of puberty, with the increased requirements of growth and activity. Cyanosis and dyspnea almost always preceded loss of consciousness, though, rarely, some patients had loss of consciousness without any such preceding symptoms. In individual patients the number of such attacks varied from 1 in a lifetime to 15 or 20 a day.

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* References 1-6.

In many of the children the history of "stiffening" or "eyes rolling," without loss of consciousness or convulsive clonic movements, was obtained. They were not included in the tabulation.

Incidence of loss of consciousness in the various forms of congenital heart disease is given in Table 1.

One hundred nine patients had at least one convulsion. This incidence was doubled in patients with tetralogy of Fallot and transposition. In these conditions the commonest type of seizure was precipitated by a very severe cyanotic and dyspneic attack. Isolated convulsions, as well as idiopathic epilepsy, accounted for the remainder of the seizures recorded (Table 2).

II. Cerebral Abscess

There were 27 cases of cerebral abscess in our series. With one exception, all were patients with cyanotic heart disease. All patients had cardiac abnormalities which permitted venous blood to reach the systemic circulation without first passing through the pulmonary circulation. Only one case followed subacute bacterial endocarditis. In the 26 others no proof of a coexistent or preexistent cardiac infection was found. Table 3 gives the distribution of these abscesses. In this hospital cerebral abscess complicating congenital heart disease has not been seen below the age of 2 years.

III. Cerebrovascular Accidents

Seventy-two patients suffered cerebrovascular accidents. Four of these had two such accidents. The distribution of these cases is given in Table 4. The incidence was significantly greater in patients with transposition of the great vessels.

IV. Mental Retardation

Criteria for the diagnosis of mental retardation were difficult to select. Motor development is so often delayed in children with cyanotic heart disease that the physical milestones of early childhood lose much significance. Progress through school is retarded by chronic illness and poor attendance. Since speech does not seem to be affected by cyanotic heart disease alone, this was considered a most reliable guide. Any child who did not talk by the age of 3 years was considered mentally retarded. In retrospective analysis of the older children this criterion seemed quite reliable.

There is an almost twofold increase of mental retardation in the cyanotic forms of heart disease as compared with the acyanotic group.

Fifteen of these patients were Mongolian idiots, and six were microcephalic idiots. Table 5 shows the distribution of such patients.

V. Incidental Conditions

Eleven patients were deaf. Six of these patients had a patent ductus arteriosus, and in these the history of rubella in the first trimester of pregnancy was elicited. (Mental retardation and cataracts were also noted in some of these patients.)

Four patients had congenital unilateral facial paralysis associated with congenital abnormalities of the homolateral external ear and cleft palate. All had tetralogy of Fallot.

There were two instances each of meningitis, otitic hydrocephalus, progressive hydrocephalus, and brain tumor.

One case of each of the following conditions was also seen in this series: measles encephalomyelitis, paraplegia, ataxia following the use of streptomycin, gargoylism, Bell's palsy, arthrogryposis multiplex congenita, poliomyelitis, amaurotic familial idiocy, progressive retinal and cochlear degeneration, syringomyelia, cerebral emboli secondary to subacute bacterial endocarditis, and cerebral angioma.

Comment

In the incidence of loss of consciousness and convulsive disorders there is a significant difference between the patients with transposition, tetralogy of Fallot, and truncus arteriosus, on the one hand, and those

TABLE 1.—*Incidence of Loss of Consciousness in Patients with Congenital Heart Disease*

Form of Congenital Heart	No. of Cases with Loss of Consciousness	Total No. of Cases	Percentages (When Significant)
Group I			
Tetralogy of Fallot	178	1045	17.4
Tricuspid atresia	4	18	...
Single ventricle	2	10	...
Transposition with pulmonary stenosis	1	16	...
Single ventricle with pulmonary stenosis	3	10	...
Truncus arteriosus with decreased flow	13	94	13.9
Group II			
Transposition	13	109	11.9
Transposition with tricuspid atresia	0	4	...
Group III			
Ebstein's malformation	0	19	...
Pure pulmonary stenosis	1	110	0.9
Truncus arteriosus with normal flow	0	10	...
Group IV			
Eisenmenger's syndrome	12	123	9.8
Truncus arteriosus with increased flow	0	10	...
Group V			
Interventricular & interauricular septal defects	0	138	0.0
Patent ductus arteriosus	0	159	0.0
Total	227	1875	12.1

TABLE 2.—*Incidence of Convulsions in Patients with Congenital Heart Disease*

Form of Congenital Heart	No. of Cases with Convulsions	Total No. of Cases	Percentages (When Significant)
Group I			
Tetralogy of Fallot	71	1045	6.8
Tricuspid atresia	2	18	...
Single ventricle	0	10	...
Transposition with pulmonary stenosis	1	16	...
Single ventricle with pulmonary stenosis	0	10	...
Truncus arteriosus with decreased flow	6	94	6.1
Group II			
Transposition	8	109	7.4
Transposition with tricuspid atresia	1	4	...
Group III			
Ebstein's malformation	1	19	...
Pure pulmonary stenosis	3	110	2.7
Truncus arteriosus with normal flow	0	10	...
Group IV			
Eisenmenger's syndrome	6	123	4.9
Truncus arteriosus with increased flow	0	10	...
Group V			
Interventricular & interauricular septal defects	5	138	3.6
Patent ductus arteriosus	5	159	3.1
Total	109	1875	5.8

TABLE 3.—*Incidence of Cerebral Abscess in Patients with Congenital Heart Disease*

Form of Congenital Heart	No. of Cases with Brain Abscess	No. of Cases Age 2 or Over	Percentages (When Significant)
Group I			
Tetralogy of Fallot	13	931	1.4
Tricuspid atresia	2	18	..
Single ventricle	1	10	..
Transposition with pulmonary stenosis	1	16	..
Single ventricle with pulmonary stenosis	1	11	..
Truncus arteriosus with decreased flow	0	76	..
Group II			
Transposition	1	60	1.7
Transposition with tricuspid atresia	0	2	..
Group III			
Ebstein's malformation	1	19	..
Pure pulmonary stenosis	2	96	2.1
Truncus arteriosus with normal flow	0	10	..
Group IV			
Eisenmenger's syndrome	2	116	1.7
Truncus arteriosus with increased flow	2	8	..
Group V			
Interventricular & interauricular septal defects	1	138	0.7
Patent ductus arteriosus	0	139	0.0
Total	27	1684	1.6

TABLE 4.—*Incidence of Cerebrovascular Accidents in Patients with Congenital Heart Disease*

Form of Congenital Heart	No. of Cases with Cerebrovascular Accidents	Total No. of Cases	Percentages (When Significant)
Group I			
Tetralogy of Fallot	41	1045	3.9
Tricuspid atresia	2	18	..
Single ventricle	0	10	..
Transposition with pulmonary stenosis	2	16	..
Single ventricle with pulmonary stenosis	1	10	..
Truncus arteriosus with decreased flow	1	94	1.1
Group II			
Transposition	12	109	11.0
Transposition with tricuspid atresia	0	4	..
Group III			
Ebstein's malformation	3	19	..
Pure pulmonary stenosis	6	110	5.5
Truncus arteriosus with normal flow	0	10	..
Group IV			
Eisenmenger's syndrome	3	123	2.4
Truncus arteriosus with increased flow	0	10	..
Group V			
Interventricular & interauricular septal defects	0	138	0.0
Patent ductus arteriosus	1	159	0.6
Total	72	1875	3.8

TABLE 5.—*Incidence of Mental Retardation in Patients with Congenital Heart Disease*

Form of Congenital Heart	No. of Patients Mentally Retarded	No. of Cases Age 3 Yr. or More	Percentages (When Significant)
Group I			
Tetralogy of Fallot	68	868	7.8
Tricuspid atresia	1	17	..
Single ventricle	1	9	..
Transposition with pulmonary stenosis	1	13	..
Single ventricle with pulmonary stenosis	1	11	..
Truncus arteriosus with decreased flow	8	63	12.9
Group II			
Transposition	9	51	17.7
Transposition with tricuspid atresia	0	2	..
Group III			
Ebstein's malformation	0	19	..
Pure pulmonary stenosis	4	90	4.4
Truncus arteriosus with normal flow	0	10	..
Group IV			
Eisenmenger's syndrome	5	113	4.4
Truncus arteriosus with increased flow	0	8	..
Group V			
Interventricular & interauricular septal defects	3	115	2.6
Patent ductus arteriosus	6	130	4.6
Total	107	1619	6.6

with pure pulmonary stenosis, septal defects, and patent ductus arteriosus, on the other. The major difference between the two groups seems to be that in pure pulmonary stenosis, patent ductus arteriosus, and septal defects there is no physiological potentiality for large, rapid variations in the amount of venous blood reaching the systemic circulation.

The history of cyanosis and dyspnea, preceding loss of consciousness or convulsions, strongly suggests that these episodes are caused by a sudden hemodynamic shift, with more venous blood now reaching the systemic circulation. The incidence of loss of consciousness and convulsive disorder in the various forms of congenital heart disease is strong evidence in favor of this hypothesis.

Cerebral abscess was seen in almost every type of congenital heart disease, except patent ductus arteriosus, included in this paper. The incidence appeared to be the same in all forms. All had in common an anatomical opening which could permit venous blood to by-pass the pulmonary capillary circulation. (The two patients with pulmonary stenosis had a patent foramen ovale.) This venous-arterial shunt which enables the pulmonary capillary bed to be by-passed seems most important, as cerebral abscess is increased in frequency in patients without congenital heart disease where such a shunt is present, i. e., pulmonary arteriovenous fistula.[8] Wood[9] has repeatedly emphasized the effective and protective role of the pulmonary and systemic capillary bed, as well as the reticuloendothelial cells of the splenic and hepatic sinusoids, in removing bacteria from the blood stream; and the removal of this safeguard in patients with such a shunt probably plays a major contributory role in the pathogenesis of these cerebral abscesses.

Cerebrovascular accidents appeared to be significantly commoner in patients with

transposition of the great vessels and tricuspid atresia. These are the two severest forms of cyanotic heart disease in the first year of life. This is the period when hemiplegias are most likely to occur.

It was difficult to assess the importance of the incidence of mental retardation. Severity of cyanosis or hypoxia did not seem to be of major significance, since neither precluded normal mental development in most patients. Associated abnormalities in the central nervous system were most important. There were 15 Mongolian idiots and 6 microcephalic idiots in the series.

Summary

The records of 1875 patients with congenital heart disease are reviewed. Of these, 481, or 25.4%, have signs or symptoms of neurological disorders.

The history of loss of consciousness or convulsions is present in 14.7% to 24.2% of the cases with cyanotic heart disease in which there is the anatomic and physiological potentiality for a rapid variation in the amount of venous blood reaching the systemic circulation. This is in contrast to an incidence of 3.1%-3.6% in other forms of congenital heart disease.

The incidence of cerebral abscess is relatively constant in all forms of congenital heart disease in which it is anatomically possible for venous blood to reach the systemic circulation without passing through the lungs.

The incidence of cerebrovascular accidents is highest in the types of congenital heart disease that tend to be severest in the first few years of life, i. e., transposition of the great vessels and tricuspid atresia.

The incidence of mental retardation is higher in patients with congenital heart disease of the cyanotic type than in the acyanotic group, or in the general population. The factors underlying this difference are not clear, but it does not appear to be hypoxia per se.

Dr. Helen Taussig and the members of the Cardiac Clinic permitted access to these patients and their records and gave us advice in this study.

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Long-Term Effects of Phensuximide (Milontin)

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Davidson, Lombroso, and Markham [1] have reported the effect of phensuximide (Milontin) in a group of 249 patients seen in the Seizure Unit of the Children's Medical Center in Boston. Their evaluation was completed in June, 1953, at which time their patients had been receiving phensuximide for one to three years. Zimmerman,[2] who pioneered in the use of this drug, reported that after an interval of 15 months the percentage of completely controlled cases had dropped from 30 to 21.[3] Therefore, we deemed it wise to restudy the longer-term effect of medication and to check the occurrence of microscopic hematuria observed by Millichap.[4]

Method of Study

All patients had been seen, as clinic or office patients, in the Seizure Unit, when first placed on phensuximide. Most of them have been followed regularly since that time. As mentioned in the report of Davidson and associates,[1] the series is heavily weighted on the side of youth, with consequently a greater occurrence of petit mal and, in the electroencephalogram, of spike-wave complexes than would be the case for an adult series.

The patients who still received phensuximide were interviewed, examined, and given an electroencephalogram, blood count, and urinalysis. The few patients who could not return personally were asked to fill out a questionnaire and send reports of their latest blood count and urinalysis. These evaluations were completed during the summer of 1955. For the patients no longer receiving phensuximide, information was obtained from their clinical records. When the succinimide failed to yield definite improvement, other treatment was substituted; when the succinimide effect was doubtful, it was discontinued and resumed only if the seizure state worsened. As in the evaluation of Davidson and associates,[1] the patients have been divided into three groups according to their response to the medication. When the number of seizures was reduced by 90% or more, the results were classified as "excellent." When the number of seizures was reduced by 50% to 90%, the results were considered "good," while they were called "poor" if the reduction was by less than 50%. The daily number of seizures prior to and during phensuximide treatment was recorded by the patients or their parents on a mimeographed sheet, where side-effects of the drug were also noted.

The daily dose ranged from 0.5 to 5 gm.; a few patients took more than 4 gm., one even 8 gm., daily. The medication was increased until seizure control was obtained or symptoms of toxicity appeared. The majority of good results occurred with doses of between 1.5 and 3 gm. The maximum amount used in the previous study was 5 gm.

Results

The over-all results in the first two groups, in comparison with those of 1953, appear in Figure 1.

Results for each of three types of seizures are tabulated separately (petit mal, 158 cases; grand mal, 114 cases, and focal seizures, 117 cases). Because many patients were subject to more than one form of seizure, the sum of the patients exhibiting the different seizure types exceeds the actual number of patients. Results for each seizure type are represented by two columns, one for results in 1953 and the other for results in 1955. Percentage figures are indicated within and at the top of the columns. Black areas represent excellent, and hatched areas good, results.

The two columns at the right represent the over-all degree of improvement. For the

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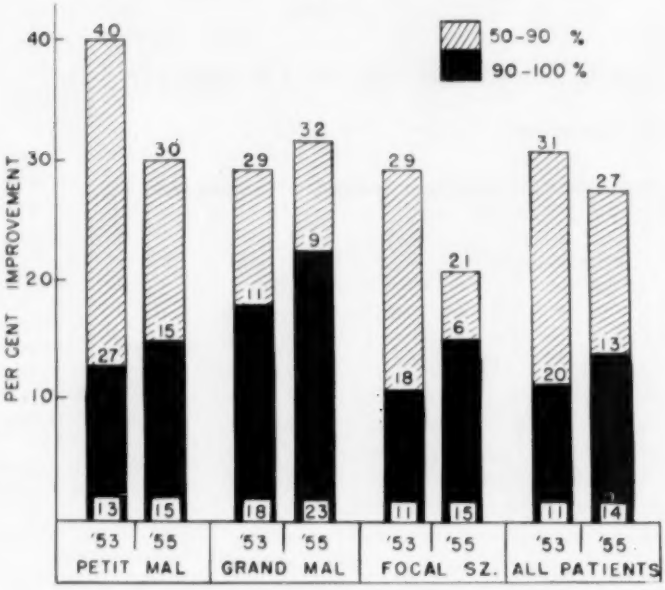

Fig. 1.—Degree of seizure control with phensuximide (Milontin). Results reported by Davidson and associates for a period ending in 1953, as compared with a follow-up period, which covers two years more. Patients number 249. Types of seizures and incidence are as follows: pure petit mal, 158; grand mal, 114; focal seizures, including psychomotor, 117; a total of 389 seizures. Percentages appear within or above the columns.

two periods of time, improvement greater than 50% was obtained in, respectively, 31% and 27% of the patients. Zimmerman [3] reported a somewhat greater drop, 30% to 21%; but his results refer to complete control. Our cases with complete or nearly complete control formed only 11% of the total in 1953 and 14% in 1955. In 1955 the proportion of excellent results was increased above that of 1953, while the proportion of good results was decreased. This finding applied not only to the over-all condition of patients but also to the individual types of seizures. With respect to excellent results (black area) the gain was greatest for grand mal, 5%, and least for petit mal seizures, only 2%. With respect to good results (hatched area) both petit mal and focal seizures lost 12 percentage points in the two-year-period; but grand mal lost only 2 points.

Prediction of Long-Term Benefit

Were results obtained in the initial trial prognostic of the long-term value of medication? How permanent is the control that may be obtained? Full answer to these questions must await the passage of years. However, the present study seems to provide some immediate evidence. The degree of control (excellent, good, or poor) as obtained in 1953 was compared with the control attained in the same persons two years later. Results are shown in Figure 2, in which, in addition to the markings of Figure 1, dotted areas indicate relatively poor control. Thus, the three columns at the left pertain to the status of persons, whose seizure control in 1953 was excellent. This could not be improved upon; hence, the change, if any, was to a lower degree of control. Three-fourths of the cases maintained their excellent rating. In 14%, 12%, and 14%, respectively, of the petit mal, grand mal or focal, and over-all cases the degree of control dropped from excellent to good; and in 5% and 4%, respectively, of the petit mal and over-all cases the degree of control fell to poor. The reciprocals of numbers at the top of columns, namely 5%, 12%, and 7%, represent cases in which results were unsatisfactory and phensuximide had been discontinued in favor of other drugs.

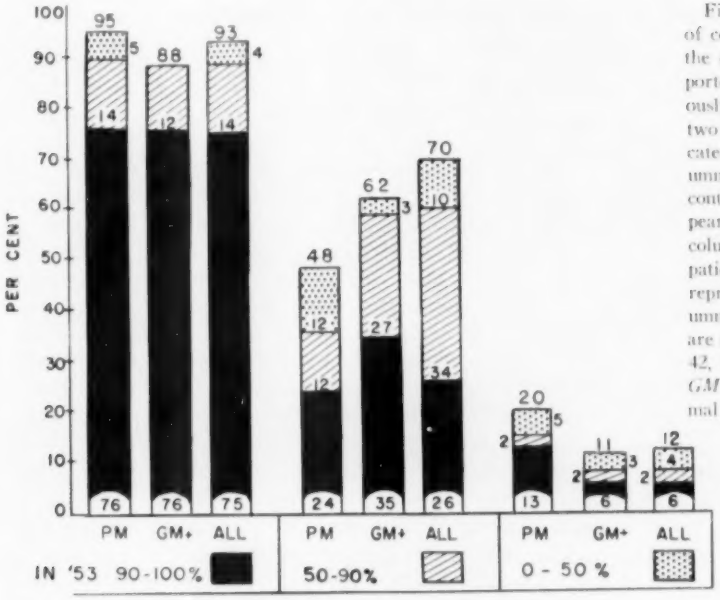

Fig. 2.—Present degree of control with respect to the degree of control reported two years previously. The control as of two years ago is indicated at the bottom; columns refer to present control. Percentages appear within and above the columns. The number of patients in each category represented by the columns, from left to right are as follows: 21, 33, 28; 42, 34, 50; 95, 164, 171. *GM+* refers to grand mal and focal seizures.

The groups with good control two years before (three middle columns) had opportunity to improve their status to a standing of excellent. Many (black portion of the columns) took advantage of this, the grand mal or focal groups to the rate of 35% and the petit mal to 24%. Regression to poor control (dotted areas) took place in 12% of the petit mal cases, as against only 3% of the convulsive cases. Thus, long-term results for convulsive cases were better than for petit mal cases. The reciprocal percentage that represented transfer to other medicines was greatest (52%) for the petit mal type seizures, 38% for the convulsive type, and 30% for the status of persons as a whole. However, with reference to maintenance of excellent or good control after phensuximide was withdrawn, 14% of petit mal patients maintained this status, as against 1.5% of patients with grand mal or focal seizures.

Next we deal with those cases in which the response to the initial use of phensuximide was poor (last three columns of Figure 2). Fifteen per cent of petit mal cases and 8% of grand mal, focal, and over-all cases advanced their status (solid plus hatched portions of the columns); 5%, and 4%, respectively, showed slight improvement (dotted area) and continued to use phensuximide, but the overwhelming majority, namely 80%, 89%, and 88%, respectively, gave up and undertook other treatment. Even a cursory view of Figure 2 emphasized that the initial results gave a strong prediction of the long-lasting effect of medication.

Phensuximide was originally given as an experimental drug to patients who, for the most part, had been resistant to a variety or drugs. Now that phensuximide is out of the experimental stage and is given more frequently as the initial medication, data should demonstrate a greater degree of excellent or good results. Phensuximide was found by Davidson and his co-workers[1] more frequently effective in patients who had not been treated than in those resistant to dione therapy (39%, as against 14% "excellent" results). Only 31 out of 158 patients with petit mal received phenosuximide without prior use of the dione. It is, therefore, not surprising that of the 99 who

were given other drugs with or after trial of phenosuximide, only 8 responded in some degree to trimethadione U. S. P. (Tridione) alone or in various combinations. A number of patients were subject to both convulsions and petit mal. Patients with generalized convulsions responded slightly better to phensuximide if 3-per-second spike-wave patterns were present in the electroencephalogram.

Other Findings

Phensuximide seems not to influence the electroencephalographic abnormalities. Many patients with perfect clinical control continued to show the same abnormality as existed prior to treatment. Because of the report by Millichap [4] of renal damage due to phensuximide, the urine was examined in 79 of our patients. In none did we find microscopic evidence of hematuria or other abnormality of the urine. Repeated blood counts also failed to show any disturbance. In addition to the 5% to 10% with mild side-effects reported by Davidson and associates,[1] nine patients reported symptoms in the two-year follow-up period. These symptoms consisted usually of drowsiness, anorexia, occasional headaches, or dysuria. Only one patient with urinary frequency and burning had to discontinue medication because of this side-effect.

Our study does not allow comparison of the effect of phensuximide with that of trimethadione. Zimmerman [5] obtained "practical" control of petit mal in 51% of cases given phensuximide and in 72% of those given trimethadione. However, contrary to our experience with trimethadione, phensuximide seems to benefit seizures of cortical origin. This is in agreement with animal experiments conducted by Funderburk and Woodcock,[6] who found that both trimethadione and phensuximide had a sedative effect on the brain-stem reticular formation; but phensuzimide was more potent than trimethadione in suppressing cortical afterdischarge.

Summary

This paper is the report of a follow-up study after two years of a group of 249 patients given phensuximide (Milontin) in treatment of epilepsy. The initial report based on from one to three years' experience, was made by Davidson, Lombroso, and Markham. Results have not been as satisfactory as those reported by Zimmerman; for example, he obtained "practical" control in 51% of petit mal patients; we did so in only 15%. He perhaps used more previously untreated patients than we did. Results are tabulated for three different types of seizures and for the over-all status of patients. In each of the four categories the number that attained a 90% to 100% control of attacks was greater at the end of the two-year period than at its beginning. The gain was small, from 2 to 5 percentage points. However, in each category there was a decrease in the number of patients with from 50% to 90% improvement. With respect to over-all benefit, patients with an improvement greater than 50% fell from 31% to 27% in the period of two years.

Changes in the degree of control in the two-year period were tabulated on the basis of the degree of initial control. In general, early improvement correlated with continued improvement. Seventy-six per cent of petit mal patients with initial excellent control maintained that position two years later, and 25% of these had stopped their medication. Maintenance for those with grand mal or focal seizures was 75% also, but only 3% had stopped the phensuximide. Among those with initially good control, 35% of grand mal or focal cases and 24% of petit mal cases had achieved excellent control by the time of this study. Thus, benefit of treatment was prompter and more lasting for petit mal, but convulsive attacks tended to improve with time. If initial improvement was less than 50%, very little was gained by a longer trial.

Conclusions

In our experience, trimethadione U. S. P. (Tridione) is more likely to produce dra-

matic control of pure petit mal than is phensuximide (Milontin). However, it carries a small risk of bringing on convulsive attacks or harmful side-effects. Phensuximide seems to be without serious side-effects and has a beneficial effect on grand mal and focal seizures, as well as on petit mal. There is some loss of effectiveness for some persons with passage of time, but probably the loss is no greater than that for other antiseizure remedies.

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Motivational Determinants in Modification of Behavior by Morphine and Pentobarbital

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Many statements in pharmacological literature imply that most drugs exert invariable effects. When differences in the effects of administering the same amount of a drug to different patients have occurred, they have usually been ascribed to "idiosyncratic" reactions. This is undoubtedly true in the case of those persons who consistently display an unusual reaction to a drug regardless of the conditions under which it is administered. However, the concept of "idiosyncrasy" cannot explain the commonly observed clinical fact that some drugs exert widely different effects upon the same patient in different situations.

The popular description of drugs as either "stimulant" or "depressant," in view of such variability, appears to stem from two sources. One is the information about drug actions, which has been obtained largely in the course of treatment of patients in the relatively standardized situation of the general hospital. The other is knowledge obtained in the laboratory. On the basis of inference from concepts of inhibition and facilitation of one neural structure by the activities of others, levels of integration and sites of action are postulated to explain the observed difference in the effects of a given drug under varied laboratory conditions.

In pharmacology, these concepts have had a considerable degree of predictive utility, especially in regard to the effects of drugs upon the activities of isolated organs or organ systems.[1] However, clinical experience has indicated that, in respect to human behavior, the specificity of action of drugs cannot be delineated solely in terms of such actions. It is becoming apparent that if one is to predict the effects of drugs upon human behavior in general, it must be recognized that there are participating variables other than those which are restricted to the organism and the drug.

That incentives may function as such variables was suggested by the results of a previous study in which it was demonstrated that the effects of morphine and pentobarbital on reaction time were changed by experimental manipulation of electric shock penalties for slow responses.[2]

Nevertheless, under identical incentive conditions, the effects of morphine differed sharply from those of pentobarbital. On the basis of these and other data,* the general thesis is proposed that motivational factors are partial determinants of the behavioral effects of drugs, and that the demonstration of drug specificity requires the control of such motivational factors.

To test these hypotheses, the effects of morphine and pentobarbital on simple reaction time were measured under four different rewarding, rather than penalizing, incentive conditions. The subjects were drawn from a relatively homogeneous population, and the same amounts of drugs were administered under each condition. The sources of variability were thus limited chiefly to differences in incentive level and the administered drugs.

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* References 1, 3, 4, 10, 11.

Methods and Materials

Subjects.—One hundred eighty-two former morphine addicts served as subjects for this study. All were prisoners serving sentences for violation of the Federal Narcotic Law. All patients volunteered for the experiments. Persons who applied were screened by a committee consisting of members of the hospital staff who were not carrying on research, to determine whether permission for participation in the experiments should be granted. Criteria for selection were as follows: age, 25 years or more; a long antisocial record, including repeated relapses to use of opiates after treatment; no significant physical defect; no evidence of psychosis; a very poor prognosis for continuing abstinence from drugs after discharge. Eligibility for participation in the experiments ceased at least six months prior to the patients' discharge date in order to provide a period of total abstinence from drugs plus rehabilitative treatment longer than that advised for nonprisoner patients. These safeguards were necessary because, as will be shown later, the extremely high value that morphine has for such a population was used to control and manipulate motivation.

Apparatus and Procedure.—The apparatus and procedure, in general, were the same as those used in three previous studies.† Manual reaction times, in milliseconds, were recorded by a modified Dunlap chronoscope when the subject pressed a key in response to the flash of a neon bulb; a Stoelting electronic chronoscope was used for calibrating the Dunlap instrument. The response key and four neon bulbs were mounted in vertical alignment on an opaque screen, ¾, 10, 15, 16, and 17 in. (1.0, 25.5, 38, 40.5, and 43 cm.), respectively, above a table. The subject was told that the bulbs would be lit in an "on your mark," "get set," "go" sequence. The lowest light indicated that a trial was beginning. The second bulb from the top flashed two seconds later and indicated that the subject should prepare for a quick response. The other two lights, one slightly above and one slightly below the "get set" bulb, were the stimulus lights. Only one of the stimulus bulbs was lit for any one trial, the subject responding to either by quickly moving the key to the left. The delay time, or foreperiod between the warning and the stimulus light, varied from one to three seconds in a predetermined random order.

When a drug was used, 15 mg. of morphine sulfate or 250 mg. of pentobarbital sodium was given intramuscularly 50 minutes before starting the test. The subjects were not informed of the nature of the drug administered.

The experimental design provided for the measurement of the effects on reaction time of two independent variables, type of drug and level of incentive. A factorial design of this nature makes possible not only the determination of the effect of each treatment independently but also the effect of various treatment combinations.[5] The formal design illustrated in Table 1 gives the number of subjects used in each treatment combination (italic figure in upper right corner of each cell). Although all the subjects were not available at one time, all were drawn from a common population, and assignment to each of the treatments was random.

It will be observed that separate control, morphine, and pentobarbital subgroups were tested under low, standard, and high incentive, and the high-incentive subgroups were retested under standard incentive conditions.

The method of changing morphine rewards proved to be an extremely powerful means of modifying the subjects' behavior. All subjects received morphine for participating in the studies, but the amount and the conditions under which they received it were varied. Subjects in the low-incentive subgroups were given their morphine rewards at least one week prior to the test day, and all received the same amount. Many of the subjects interpreted this prior reward as a gratis allowance, even though it was made explicit that cooperation on the subsequent test would be re-

TABLE 1.—*Reaction Time Means and Number of Subjects on Each Treatment Combination*

Drug Treatment	Incentive Treatment			
	Low	Standard I	High	Standard II
Control (no drug)	206 *14*	190 *16*	171 *36*	160 *12*
Morphine	188 *14*	195 *16*	171 *55*	180 *12*
Pentobarbital	233 *14*	201 *16*	160 *24*	155 *12*

† References 2-4.

quired. Two of these subjects did not report on the test day. Although the others were sufficiently cooperative to complete the test, their attitude was generally poor; several complained that they were doing the test without any reward. This behavior provided some evidence of the validity of the low-motivation condition.

When Standard I Incentive was employed, all subjects were given the same amount of morphine reward, but they received it after they had completed the test.

Under High Incentive the reward was received after completion of the test, but the amount of morphine reward was made contingent upon "fast" reaction times. The more quickly subjects responded the greater was the amount of morphine they earned. A scoring device placed on the upper right corner of the screen showed the subjects the amount of their earnings for each response and the total earnings for each series. These procedures developed an extremely high degree of cooperation and, as might be expected, considerable competition among the subjects.

Procedures used for the fourth incentive treatment, indicated in Table 1 as Standard II (post-High-Incentive retest), were essentially the same as those used for Standard I Incentive. The amount of morphine reward was the same for all subjects and was received after the completion of the tests. The difference between Standard I and Standard II conditions was that in the former, independent groups were used, whereas in the latter, subjects that had previously performed under High Incentive were utilized. In addition, Standard II subjects were given more knowledge of their performance.

As indicated, three subgroups, labeled Control (no drug), Morphine, and Pentobarbital, were tested under each of the four incentive conditions. Four series of reaction times were obtained on all subgroups. The series consisted of 18 reactions each and were spaced at 15-minute intervals. (Chart 1).

Treatment of Data.—In obtaining the points shown in Chart I, mean reaction times for each subject were combined to produce subgroups means for each series. The measures used in the analyses of variance were single means for each subject; i. e., a general mean was obtained for each person over four series. The analysis of variance allows for the simultaneous comparison of several treatment effects, thus providing the basis for statements concerning the interaction of treatments—in this case interaction between drugs and incentive levels. It also reduces the possibility of falsely accepting a hypothesis when a large number of comparisons are made.

Because the over-all analysis of variance revealed significant interaction (F-4.621), analyses were made of the "simple" effects of drugs when incentives were held constant and of the effects of incentives when drugs were held constant. A

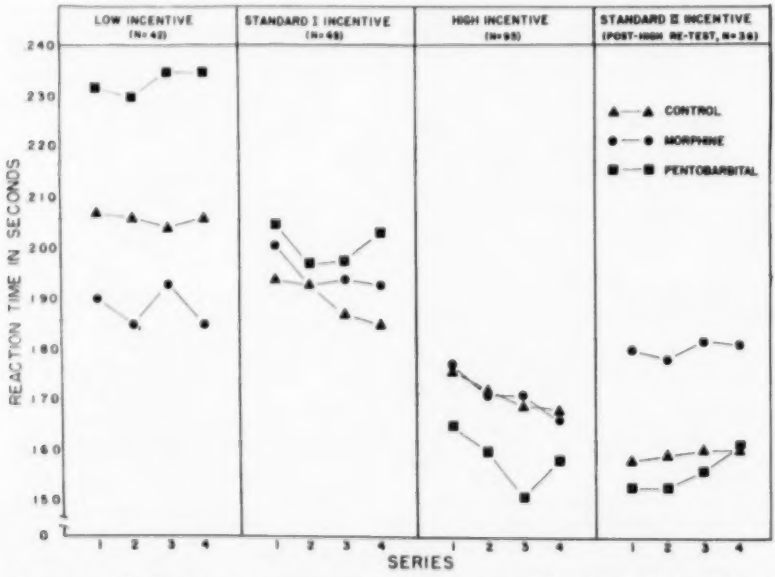

Chart 1.—Effects of drugs on mean reaction time under various levels of incentive. Each series consisted of 18 consecutive manual reactions to light flashes presented at intervals of 15-20 seconds. The four series were separated by "rest" periods of 15 minutes each.

summary of these calculations is presented in Table 2.‡ All treatment combinations that showed significant variance were further analyzed by Fisher's *t*-test to determine the significance of differences between treatment pairs that were critical to the present hypotheses.[6]

studies. Low Incentive significantly lengthened this response time, and High Incentive and Standard II Incentive significantly reduced it ($P = <0.05$, <0.01, <0.01, respectively).

TABLE 2.—*Summary of Analysis of Variance: "Simple" Effects of Treatments*

Mean Squares for Incentives								
Source	*df*	Low	*df*	Standard I	*df*	High	*df*	Standard II
Treatments	2	7,146.29	2	464.87	2	1,172.77	2	2,085.19
Within groups (W)	39	607.50	42	396.53	92	312.45	33	330.26
Total	41	926.47	44	399.64	94	330.76	35	430.54
F=Treatment Within groups		11.76		1.17		3.75		6.31
Probability		<0.001		>0.10		<0.05		<0.005

Mean Squares for Drug Conditions							
Source	*df*	Control	*df*	Morphine	*df*	Pentobarbital	
Treatments	2	6,487.96	2	3,554.38	2	24,706.77	
Within groups (W)	62	341.50	61	336.99	50	547.27	
Total	64	533.57	63	439.13	52	1,479.94	
F=Treatment Within groups		18.99		10.55		45.31	
Probability		<0.001		<0.001		<0.001	

Results

It will be observed in Table 2 and Chart 1 that under the conditions of Standard I Incentive the various drug treatments did not produce significant changes in reaction time. In contrast, however, under each of the other incentive conditions significant variance due to drug effects was obtained. Likewise, significant changes were produced by Low, High, and Standard II conditions when the drug treatments were constant. Each of the *F*-ratios reached at least the 5% level of confidence. The outcome of the *T*-tests in regard to the significance of treatment pairs is shown in Table 3.

When considering no-drug (control) measures (Tables 1 and 2, Chart 2), it was found that Standard I conditions produced reaction time that approximated quite closely those obtained on other similar

With regard to the effects of morphine under different levels of incentive, it is observed that in comparison with Standard I Incentive, Low Incentive produced no significant change in reaction times and that High Standard II significantly reduced them ($P = >0.10$, <0.01, <0.05, respectively).

In examining the effects of pentobarbital under different levels of incentive, it is observed that in comparison with Standard I Incentive, Low Incentive produced very significant lengthening of reaction times, and that High and Standard II produced very significant decreases ($P = <0.01$, <0.01, <0.01, respectively).

When considering results under each of the various incentive levels separately (Chart 1), it is seen that the order of the drug subgroups changed radically: Under Low Incentive the order of increasing reaction times was morphine, control, pento-

‡ A separate analysis was made of the Standard II Incentive results, since an independent subgroup was not used on this condition.

TABLE 3.—*Comparison of Mean Reaction Times, in Seconds, for Various Treatment Combinations*

	M_1	M_2	Diff.	S.E. Diff.	t	P
Control (no drug)						
Standard I *vs.* Low	0.190	0.206	0.016	0.0078	2.05	=0.05
Standard I *vs.* High	0.190	0.171	0.019	0.0061	3.12	<0.01
Standard I *vs.* Stan. II	.190	0.160	0.030	0.0075	4.00	<0.01
Morphine						
Standard I *vs.* Low	0.195	0.188	0.007	0.0067	1.05	>0.10
Standard I *vs.* High	0.195	0.171	0.024	0.0055	4.36	<0.01
Standard I *vs.* Stan. II	0.195	0.180	0.015	0.0072	2.08	<0.05
Pentobarbital						
Standard I *vs.* Low	0.201	0.233	0.032	0.0109	2.94	<0.01
Standard I *vs.* High	0.201	0.160	0.041	0.0067	6.12	<0.01
Standard I *vs.* Stan. II	0.201	0.155	0.046	0.0075	6.13	<0.01
High Incentive						
Morphine *vs.* control	0.171	0.171	0.000	0.0050	0.00	>0.10
Pentobarbital *vs.* control	0.160	0.171	0.011	0.0045	2.44	<0.05
Low Incentive						
Morphine *vs.* control	0.188	0.206	0.018	0.0079	2.28	<0.05
Pentobarbital *vs.* control	0.233	0.206	0.027	0.0107	2.52	<0.05
Standard II Incentive						
Morphine *vs.* control	0.180	0.160	0.020	0.0081	2.47	<0.05
Pentobarbital *vs.* control	0.155	0.160	0.005	0.0070	0.71	>0.10

barbital ($P = <0.05, <0.05$, respectively, as compared with the control).

No significant differences appeared under Standard I conditions. Under High Incentive, the order was pentobarbital followed by control and morphine ($P = <0.05, >0.10$, respectively, in comparison with control). Under Standard II condition, the order was pentobarbital, control, and morphine ($P = >0.10, <0.05$, respectively).

As shown in Chart 2, the differences to which attention should be directed most specifically are the striking changes in relative positions of pentobarbital subgroups under Low and High Incentive and the changes in relative positions of morphine subgroups under Low and Standard II conditions.

Comment

The results demonstrate clearly that some effects of drugs on behavior can be quite dependent upon the incentive conditions under which they are used. In our study, the pharmacological effects of morhpine and pentobarbital were specific, but each drug facilitated, retarded, or had no effect on performance, depending upon the level of incentive.

If only the procedure of Standard I Incentive was used by an investigator, he might report that neither morphine nor pentobarbital produced a significant effect on this type of performance (Chart 1). If he used the procedure of Low Incentive only, he would report that the results were a classic example of the depressant action of barbiturates, but he would also report that morphine was a stimulant. If he employed only High Incentive, he would state that morphine had no effect and that pentobarbital was a stimulant, facilitating this

form of behavior. Or, again, if he used only procedures of Standard II Incentive, he would class morphine as a depressant and pentobarbital as neutral in action, producing no effect.

From another viewpoint, the data indicated that changes in the level of incentive produced marked changes in performance within each of the drug conditions ("control," "morphine," or "pentobarbital"). As shown by the *F*-ratios in Table 2 and by substantial change in behavior of morphinized subjects.

It is seen that if specificity of drug action on behavior occurs, at least part of it is due to the class and level of incentives of the particular situation. The converse is also shown. If changes in performance occur under various incentives when a certain drug is used, part of the change is attributable to specificity of action of the particular drug. Thus, the action of morphine

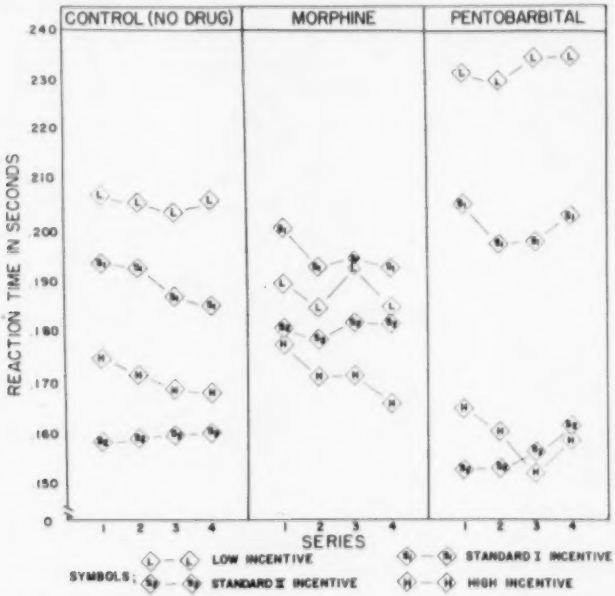

Chart 2.—Effects of incentives on mean reaction time under various drug conditions. "Series" as in Chart 1.

inspection of Chart 2, changing incentives produced a much greater effect when subjects were tested under pentobarbital than when tested under either of the other conditions; reaction times of Low Incentive were much longer (slower) and those of High Incentive were shorter (faster). In regard to opiates, however, it can be seen in the same tables and charts that morphinized subjects were relatively less influenced by incentive changes than subjects under the other conditions. Only the most powerful incentives used in these experiments, namely, the possibility of obtaining more morphine (High Incentive) produced a changes from "stimulant" to "no effect" when the situation changes from "Low Incentive" to "High Incentive." In contrast, the action of pentobarbital changes from "depressant" to "stimulant" when the situation is changed in an identical manner. Consequently, it may be said that drugs do have specific actions on behavior, but that their specificity does not consist in their being "stimulant" or "depressant" under any and all conditions. Rather, their specificity refers to predictable differences in modes of action under various conditions.

Obviously, there are several different directions reasoning might take to explain

the present results. Perhaps the most fruitful approach is in terms of drug-produced changes in motivation. "Motivation" as a dynamic construct or concept is defined as a disposition or readiness to respond,§ which is inferred from observation of the changes in behavior that are exclusively correlated with altered incentives under given antecedent conditions. Thus, it is maintained that, although the behavioral effects of drugs are the consequences of physicochemical changes which they produce, the mechanisms through which such effects produce behavioral change must be analyzed not only in terms of changes in localized excitatory and inhibitory processes in the central nervous system, but also in terms of changes in motivational processes. In other words, the changes in behavior which drugs produce are due, in part, to their effects on specific motivations.

An example of altered sensitivity to specific stimulation is the contrast between the effects of barbiturates (or alcohol) and opiates on *interest* in sexual activities.‖ Former narcotic addicts, such as those that participated in the present study, state that under barbiturates such interest is enhanced, while under opiates it is practically eliminated. Similar specificity of effect of these drugs on quite a different class of responses was observed during the present study. It was noticed after injections of pentobarbital that expressions of hostility were quite common under all levels of incentive, whereas under morphine they were not.

The nature of the particular motivations that operated in our experiment cannot be determined with assurance. Since the subjects were former narcotic addicts, it may be assumed that "a desire for morphine" was the dominant motivating factor. Although morphine rewards were indeed manipulated, incentives of other sorts probably operated as well. Thus, under "High Incentive" competition for "high scores" seemed to be keen. In the course of the experiment, subjects often inquired about "how they were doing." In the "Low Incentive" situation, many of the subjects appeared to be resentful, on the grounds that they were expected to "work for nothing." Since these factors could not be controlled, further experiments with other kinds of rewards and/or punishments are needed in order to delineate more precisely the sorts of motivation that are affected by opiates, barbiturates, and other classes of drugs.

The data suggest, however, that the differences in attractiveness of drugs, for particular persons, might be partially explained on the basis that a specific drug either reduces motivation that is undesirable or enhances motivation that is desirable. Conclusions drawn from clinical and other investigations¶ in this laboratory support the further inference that the preference for opiates by certain addicts is not the result of an accidental concurrence of events. The reduction in sensitivity to pain and discomfort, to sexual objects, and to other social influences, and the concomitant enhancement of euphoria, effectively shield particular personalities from types of behavior which are undesirable to them. Probably such actions of morphine would be very restricting and, therefore, undesirable for the "normal" personality.

Even a very incomplete analysis of the effects of each major class of drugs would be very difficult. However, they might be analyzed in this manner, and the attractiveness of each drug might be rather reliably predicted on the basis of knowledge of the personality of the user and the actions of the drug on certain motivations.

Summary and Conclusions

Since the description of drugs as either "stimulant" or "depressant" did not appear to be sufficient to account for their behavioral effects, it was proposed that motivational factors must be considered as partial determinants of such effects. The present experiment, designed to test this hypothesis, was carried out on 182 former narcotic

§ References 7, 8, 9.

‖ References 10 and 11.

¶ References 13 and 14.

addicts. Visual-manual reaction times were measured on separate groups of subjects after the administration of 15 mg. of morphine sulfate or 250 mg. of pentobarbital sodium, and these were compared with the reaction times of other subjects who received no drug on the test day. Each of these measurements was made under four conditions which differed from each other with respect to the incentive (morphine reward) offered for participation in the experiments.

The results indicate that changing incentives significantly modifies control reaction time, as well as the effects of morphine or pentobarbital thereon. Thus, in comparison with the control, both drugs acted either as "stimulants" (accelerated reaction time) or as "depressants" (slowed reaction time) or had no effect, depending on the particular incentive conditions under which they were administered. The actions of these drugs, however, were "specific" with respect to each other: The effect of pentobarbital changed from "depressant" to "stimulant" when conditions changed from "Low Incentive" to "High Incentive," while the action of morphine changed from "stimulant" to "depressant" when identical changes in incentive level were made. Viewed from another standpoint, the results indicate that sensitivity to changes in incentives is reduced by morphine and enhanced by pentobarbital.

It is postulated that changes in incentive levels, manipulated by the observer, alter performance through effects on specific motivations. Hence, from the data presented, it is inferred that performance, as well as the effects of drugs thereon, is determined in part by the particular motivations that obtain when the measurements are made. The "specificity" of the effects of any particular drug will therefore be apparent only if the motivations involved in the behavior studied are controlled.

Furthermore, it is concluded that drugs exert "specific" effects on particular motivations, and that differences in the attractiveness of drugs for different persons may be partly explained on the basis that motivations acceptable to the subject can be enhanced and unacceptable ones suppressed by use of particular chemical agents.

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Pathogenesis of Trigeminal Neuralgia

A Review

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Since Nicolaus André,* of Versailles, described in 1756 paroxysmal facial pain under the term "tic douloureux," the literature on this subject has become enormous; yet even today the fundamental cause and pathophysiologic mechanism underlying trigeminal neuralgia remain obscure.

Various theories attempting to explain the nature of trigeminal neuralgia will be reviewed first, before we discuss our own concept of the disease. The mechanism responsible for tic douloureux has been localized in the trigeminal pathway anywhere from the facial skin to the endings of thalamocortical fibers; various causative factors have been incriminated, such as mechanical pressure, infectious-inflammatory lesions, and organic or functional vascular changes.

Harris [2] (1926) considered an infectious neuritis of the trigeminal nerve endings in the region of the maxilla or mandible as the main cause. He assumed this process to be mostly dental in origin, but occasionally secondary to sinusitis. Rowbotham [6] (1954) found perineural fibrosis of the terminal trigeminal filaments in skin biopsy specimens from patients with tic douloureux. Wyburn-Mason [7] (1953) expressed the view that the nerves of the cervical plexus may participate in the pain mechanism of tic douloureux by contributing to the sensory facial innervation through anastomotic branches. This author claimed that in many cases attacks of trigeminal neuralgia could be abolished by interruption of cervical nerves. Recent work by Crue, Shelden, Pudenz, and Freshwater [8] (1956) partially confirmed Wyburn-Mason's observations.

Most authors have suspected the presence of a pathologic process in the Gasserian ganglion or sensory root.

Dandy [9] (1934) found local anomalies encroaching upon the trigeminal root in 56% of his surgically verified "tic" cases; these lesions were mostly vascular malformations or abnormally placed blood vessels. He felt that this was no mere coincidence.

We had occasion to observe two cases of typical trigeminal neuralgia associated with arteriovenous malformations of the brain.

The first patient exhibited a combination of a temporo-occipital vascular malformation with an ipsilateral tic douloureux involving the third division. At operation (by a subtemporal approach) anomalous tortuous small arteries were found to be intermingled with the fibers of the sensory root.

In the second case, trigeminal neuralgia of the second division occurred contralateral to a large parieto-occipital arteriovenous angioma; here huge redundant veins surrounded extradurally the third division and the Gasserian ganglion.

Revilla [10] reported (also from Dandy's material) 34 cases of cerebellopontine-angle tumor with "tic" pain.

Even though neoplasms and vascular anomalies close to the Gasserian ganglion or sensory root are known occasionally to produce symptoms of typical trigeminal neuralgia, most authors disagree with Dandy's view that such pathologic conditions are the specific morphologic cause of ordinary tic douloureux. Olivecrona [11] (1941) suggested that trigeminal neuralgia may be mechanically caused by pressure and traction on the sensory root. He pointed out that

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* André, N., cited by Krause.[1]

even under normal conditions the trigeminal root is slightly stretched and angulated over the petrous apex as the fifth nerve takes a caudad course toward its entrance into the brain stem. Since the spine is shortened in aged persons, and, therefore, the brain tends to sag toward the foramen magnum, this stretching of the fifth nerve is increased, and thus trigeminal neuralgia may develop. Taarnhøj [12] (1952) concluded from the success of his operation that compression of the sensory root by a tight dural ring may be the significant etiologic factor. According to Gardner's [13] complicated hypothesis (1953), sensory root fibers become demyelinated by mechanical compression at the petrous crest and thus may permit short circuiting of impulses. Gardner assumes that efferent autonomic impulses originating from the mesencephalic trigeminal nucleus are activated by tactile stimuli and that these autonomic impulses become misdirected into the pain fibers within the sensory root.

Since trigeminal neuralgia mainly affects the older age group, many clinicians have attributed the disease to circulatory disturbances of the Gasserian ganglion or root. Doering and Magun [14] adduced statistical evidence of a greater incidence of arterial hypertension in "tic" patients than in the average population of the same age. The same authors described histologic changes in the basket fibers surrounding the nerve cells of the Gasserian ganglion, supposedly due to arterial hypertension. Schaltenbrand [15] (1953) found arteriosclerotic changes in the Gasserian ganglion; he considers trigeminal neuralgia as an intermittent claudication of the ganglion and explains the pain paroxysms by a state of temporary anoxemia of the ganglion cells. A similar view was expressed by Wolff [16] (1948), who also interprets the attack of tic douloureux as an episodic ischemia of trigeminal structures. Such a situation is more likely to arise when the vascular bed is already narrowed by existing occlusive vascular disease (arteriosclerosis). Wolff believes that vasoconstriction causes the attack and supports his argument by the observation that vasoconstrictor drugs elicit or increase the pain, but vasodilators (amyl nitrite, histamine, nicotinic acid U.S.P.) suppress or diminish it. Haertel and Kulenkampff † also regard the tic paroxysm as a vasomotor crisis of the Gasserian ganglion, supposedly the result of functional autonomic disturbances.

On critical analysis, however, there is at present no sufficient evidence that organic or functional vascular change is the primary etiologic factor in trigeminal neuralgia. Although tic douloureux occurs most frequently in the older age group, which is commonly afflicted by vascular disorders, a causal relationship between arteriosclerotic-hypertensive vascular disease and tic douloureux has not yet been definitely established. If tic douloureux were caused by an ischemic crisis in the Gasserian ganglion, one would expect trigeminal neuralgia occasionally to follow cervical carotid occlusion (either by surgical ligation or spontaneous thrombosis, especially in older people), but this is definitely not the case. If, on the other hand, one assumes that the pain mechanism involves trigeminal connections in the brain stem, temporary deficiency of the vertebral circulation might conceivably play a role; yet here, again, nobody has demonstrated a definite association of tic douloureux with clinical signs of impending insufficiency of the vertebral circulation, such as vertigo or tinnitus.

As to the importance of functional vascular disorders, interruption of the cervical sympathetic chain by procaine block, surgical section, or administration of sympatholytic drugs does not prevent or cure permanently tic douloureux (White and Sweet [19]). Vasodilators, such as nicotinic acid, amyl nitrite, histamine, tolazoline (Priscoline) and papaverine, have a definite though variable effect on so-called vascular headache; but, in our experience, they do

† Haertel, cited by Krayenbühl.[17] Kulenkampff.[18]

not influence to any extent the pain of true trigeminal neuralgia.

Since vasomotor mechanisms participate in thermoregulation, they respond to climatic factors. It has been noted by some clinicians that in a given patient attacks of trigeminal neuralgia seem to occur under certain meteorologic conditions. Williams[20] (Rochester, N. Y.) found in his own series of 245 cases that the attacks of neuralgia were exacerbated mostly in March and October. Mayfield,‡ of Cincinnati, observed a definite preponderance of attacks during the hot, humid periods with low barometric pressure which are so common in the Midwestern spring and early summer.

In an attempt to analyze the possible correlation of tic attacks and climatic factors, one of us (C. F. L.) made an inquiry of various neurosurgeons. Among 1024 cases of trigeminal neuralgia compiled from the Midwest and Great Lakes regions (an area of similar climatic conditions) some increase in incidence of "tic" was observed in the early summer months; however, the difference in figures was not sufficiently great to be considered statistically significant. At any rate, these experiences do not support the assumption that either vasoconstrictor or vasodilator effects of climatic changes are important in the causation of "tic" attacks.

In conclusion, then, it is our impression that the vascular factor plays no real etiologic role in trigeminal neuralgia, although it may well be a contributing element.

Some neurologists have taken the position that the pathologic process responsible for tic douloureux must be sought in the central, rather than in peripheral, trigeminal connections. Parker,[21] Harris,[5] Finesilver,[22] and others emphasized the frequent occurrence of typical unilateral or bilateral trigeminal neuralgia in multiple sclerosis and demonstrated sclerotic plaques in the central trigeminal pathways at autopsy.

Lewy and Grant[23] (1938) considered trigeminal neuralgia a partial thalamic syndrome. According to these authors, trigeminal neuralgia is characterized by an elevated threshold for cutaneous stimuli and a delayed, but explosive and prolonged, after-discharge. Lesions in the corticothalamic connections may release thalamic discharges and thus lead to recruitment of more impulses. Lewy and Grant support their theory by rather dubious clinical evidence, such as reduction of pain points in the trigeminal cutaneous area (not confirmed by others), presence of pyramidal and extrapyramidal signs, and anatomic findings, such as small vascular lesions of the ipsilateral arcuate nucleus and centrum medianum of the thalamus, lesions in the thalamocortical radiations, and ipsilateral cortical atrophy. Furthermore, they quote a clinical case of thalamic syndrome in which the facial component of pain was abolished by a peripheral trigeminal injection of alcohol (as in true tic douloureux). Of the authors who postulated a central origin of trigeminal neuralgia, Kinnier Wilson[24] (1940) conceived the tic douloureux attack as a sensory epileptiform discharge which occurs as a release phenomenon in an inhibitory efferent trigeminal system.

Not until recently has the attempt been made to investigate trigeminal neuralgia experimentally by electrophysiologic methods. King and Meagher[25] (1955) studied trigeminal potentials in the cat, after stimulation and after section of the sensory root and the spinal trigeminal tract. Their work suggests that stimulation of large touch and pressure fibers (A-fibers) in the peripheral trigeminal system activates a delayed response of small pain fibers (C-fibers) in the spinal trigeminal nucleus. In another series of experiments§ they tried to simulate in cats the clinical syndrome of trigeminal neuralgia by applying aluminum hydroxide gel to the spinal trigeminal nucleus. The animals so treated developed marked trigeminal hyperesthesia: They

‡ Mayfield, F.: Personal communication.

§ King, R. B., and Meagher, J. N.: Overreaction to Touch Stimuli in the Trigeminal Area of Cats, read at the 23d Meeting of the Harvey Cushing Society, May 17, 1955, Quebec, Canada.

avoided touch of the affected side of the face, and it was possible to evoke violent pain reactions by mild tactile stimulation.

From the review of the literature it is evident that no specific anatomic lesions have so far been discovered in trigeminal neuralgia. The fact may be significant, however, that in many of the anatomically verified cases the trigeminal pathway was found to be damaged somewhere in its course; on the other hand, similar lesions have been encountered in patients without trigeminal neuralgia. When such changes were present bilaterally in cases of unilateral tic douloureux (as in Schaltenbrand's case), they are per se unlikely to be the cause. That gross lesions, such as tumors, aneurysms, and vascular anomalies, impinging on the Gasserian ganglion or sensory root, or sclerotic plaques within the brain stem may evoke pain is not astonishing; cases of this type should be better classified as symptomatic trigeminal neuralgia. Here the pain may be paroxysmal, and in some cases even brought on by a trigger mechanism; but as a rule there exists a background of constant pain with superimposed bursts, and objective signs of focal neurologic involvement are demonstrable.

Since morphologic analysis has failed to solve the mystery of tic douloureux, we must seek the answer in a neurophysiologic approach. Trigeminal neuralgia and glossopharyngeal neuralgia are fundamentally different from all other so-called neuralgias. Their pathognomonic feature is the trigger mechanism which sets off the attack. The paroxysm of pain is precipitated either by physiologic tactile stimuli applied to a cutaneous trigger zone (e. g., touching, shaving, washing the face) or by proprioceptive stimulation, such as moving the lips, chewing, and yawning. Thermic (cold) stimuli appear to be less effective in trigeminal neuralgia but frequently elicit the pain of glossopharyngeal neuralgia. On the other hand, pain stimuli or firm deep pressure does not seem to provoke an attack. The trigger zones lie, as a rule, within the trigeminal or glossopharyngeal territory, respectively, and are confined to small cutaneous areas below the nasolabial fold and the marginal vermilion of the lower lip and at the eyebrow, or to mucosal areas at the gum lines or tonsillar region, respectively. In some cases the trigger zone is located in the territory of a branch different from that of the pain; e. g., supraorbital pain may be provoked by a nasolabial trigger or second-division pain by stretching the masticatory muscles (third-division trigger). As Crue and associates [8] have pointed out, the tic attack may be occasionally triggered off from a region supplied by nerves of the cervical plexus, or, in very rare instances, even from far-distant points of the body surface.

If afferent stimuli are no longer conducted to the center by blocking the trigger zone, the pain paroxysm is prevented. The typical attack of trigeminal neuralgia is an evoked response that occurs with a slight delay. The pain reaction is explosive, supermaximal, frequently repetitive and has a short duration (less than 30 seconds). The attack ends just as abruptly as it starts, and afterward there is characteristically a refractory period of variable duration, in which additional stimulation will not provoke further pain.

The views of various authors are divided as to where in the trigeminal system the pain mechanism is located. Theories that place the mechanism in the periphery and explain the paroxysm either by irritation of terminal fibers or by misdirection of tactile or autonomic impulses into pain fibers are unconvincing. The clinical characteristics of tic douloureux are quite different from hyperpathic pain associated with certain incomplete lesions of the trigeminal pathway (for instance, postherpetic trigeminal neuralgia). In such cases spontaneous burning paresthesias may be present; cutaneous stimulation instantaneously increases or elicits this burning hyperpathic sensation, which outlasts the stimulus and wanes gradually. The hyperpathic response

occurs after every stimulation without refractory period and may be even enhanced by repetitive excitation. Finally, an actual sensory deficit or a paradoxical response (e. g., pain sensation on thermic stimulation) can usually be demonstrated. In true tic douloureux, however, no loss of sensation can be shown by customary clinical tests. The sharp shooting electric quality of tic pain differs from the burning paresthetic hyperpathy of incomplete lesions of the sensory system.

Still another important argument speaks against a peripheral origin of tic douloureux, viz., the fact that excitation of a trigger area in one branch may evoke pain in another branch. All evidence, therefore, strongly suggests a central location of the pain mechanism. The tic attack has been compared to a convulsive type of evoked discharge and after-discharge. It appears extremely unlikely that such mechanism should be cortical, first, because the cortex is not directly concerned with pain responses and, second, because the pattern of tic pain follows the distribution of peripheral trigeminal branches. This latter point also strongly argues against a thalamic origin of trigeminal neuralgia, since it is improbable that even a small circumscribed lesion in the thalamic terminal of the trigeminal pathway (i. e., the arcuate nucleus) could account for such spatially limited pain phenomena. Consequently, in order to explain the peripheral somatotopic pain pattern, the mechanism of tic douloureux must be sought somewhere between the Gasserian ganglion and the thalamus. Similar conclusions were reached by Crue and associates, who placed the "focus" of the tic mechanism at the level of the lower brain stem.

In view of the limitations of the purely clinical approach, recent electrophysiologic studies by King and Meagher ‖ promise to shed some light on the problem. These investigators observed in cats, after afferent stimulation of a peripheral trigeminal branch, delayed multiphasic potentials in the spinal trigeminal nucleus. Such delayed responses could be recorded in the third division after afferent stimulation of the second peripheral branch, a phenomenon resembling the clinical experience that tic pain may be located in a branch different from the trigger area. The delayed response can be reduced by blocking the rapidly conducting fibers in the stimulated branch; this would suggest that pain fibers are activated by tactile or proprioceptive fibers. Some anatomic basis is available for these electrophysiologic observations: Walker [26] and Sjöqvist [27] described bifurcations of the large tactile A-fibers on entering the brain stem; their descending branches synapse in the spinal trigeminal nucleus, where the smaller pain fibers have numerous terminals. Most of the afferent trigger impulses travel in the trigeminal system, but, as suggested by Wyburn-Mason and Crue and associates, there is also evidence for an auxiliary extratrigeminal path through the upper cervical nerves. The spinal trigeminal nucleus, being a cephalic continuation of the substantia gelatinosa of Rolando, probably receives synaptic connections from the upper cervical posterior roots. From such experimental and anatomic evidence it may be proposed that also in patients with trigeminal neuralgia physiologic tactile and proprioceptive impulses reach the spinal trigeminal nucleus, where they initiate a delayed pathologic pain reaction.

The explanation of the supermaximal explosive pain response within the central trigeminal connections remains the chief problem. Again, King and Meagher's work offers a possible clue: Injection of aluminum oxide (alumina) gel into the spinal trigeminal nucleus (of cats) produced a 300%-600% increase of amplitude of the delayed potentials. Such exaggerated delayed response could be diminished by trigeminal tractotomy and abolished by section of the

‖ King and Meagher.[28] King, R. B., and Meagher, J. N.: Overreaction to Touch Stimuli in the Trigeminal Area of Cats, read at the 23d Meeting of the Harvey Cushing Society, May 17, Quebec, Canada.

posterior trigeminal root.¶ These experiments suggest, first, that a chronic central excitatory state is produced by injection of aluminum oxide gel into the spinal trigeminal nucleus, and, second, the delayed response is conducted in a centrifugal (efferent) direction back to the Gasserian ganglion and the peripheral trigeminal branches. Gardner, basing his theory on the work of Lewy, Groff, and Grant, also believes that in the cat there is activation of efferent (parasympathetic) fibers which arise from the mesencephalic trigeminal nucleus and extend through the trigeminal system to the periphery. Two clinical observations might possibly support the concept of an efferent component in the tic mechanism: 1. As already noted by Foerster,[28] the attack of pain is occasionally marked by a facial flush, a phenomenon which could be the result of excitation of efferent vasodilator fibers, or perhaps of antidromic impulses in sensory fibers. 2. Some patients feel, even after trigeminal rhizotomy, the "strike" of the attack, but without pain. This may indicate that an efferent central discharge is no longer able to activate the actual pain mechanism. Further electrophysiologic studies in humans with a normal trigeminal system and with tic douloureux are clearly needed to fill the remaining gaps in our knowledge.

In summary, it is suggested here that an attack of trigeminal neuralgia represents a pathologic multineuronal reflex in the trigeminal system of the brain stem. The extreme intensity of the delayed pain response to a mild physiologic stimulus probably is not due to a release mechanism. It may be better explained by efferent conduction of impulses from the spinal trigeminal nucleus back to the periphery; there the impulses reverberate and reexcite the central trigeminal connections, with recruitment of additional neurons. Such process of self-exciting after-discharge may be repetitive, until the firing neurons become refractory. This theory raises the question as to what causes the hyperirritability of the spinal trigeminal nucleus. Even though no specific histopathologic lesions have been demonstrated in cases of tic douloureux, morphologic changes were found frequently somewhere in the trigeminal pathway; it is conceivable that abnormal electric potentials arising in such damaged system could be responsible for an increased central excitatory state. Furthermore, the hypothesis may be advanced that senescent changes in the ganglion cells of the medullary nucleus may alter its neuronal metabolism in such a manner that the neurodynamic responses become exaggerated. The biochemical activities of neurons can be influenced by alteration of blood flow or by pharmacologic means; certain substances of the vitamin B group which possess such properties may, therefore, be useful in modifying or correcting metabolic disturbances in abnormal trigeminal neurons. There is some clinical evidence that thiamine and cyanocobalamin (vitamin B_1 and B_{12}) may have some beneficial, albeit transient, effect on trigeminal neuralgia. On the other hand, it is admittedly difficult to judge therapeutic action of drugs in a disease with a course as unpredictable as tic douloureux.

Finally, the question must be raised as to what is the rationale of surgical treatment of trigeminal neuralgia. Assuming a central pain mechanism in trigeminal and glossopharyngeal neuralgia, surgical (or chemical) interruption of the peripheral pathway is effective because it prevents the physiologic afferent impulses from activating this abnormal mechanism; for example, alcohol injection into the infraorbital nerve stops second-division neuralgia; cocainization of the mucosa in the tonsillar region will avert an attack of glossopharyngeal tic. Even section of the major auricular nerve may temporarily relieve pain, as it reduces the influx of auxiliary afferent impulses. Posterior rhizotomy and trigeminal tractotomy, however, may accomplish more than merely interrupting the afferent messages from the trigger zone. It is conceiv-

¶ King, R. B.: Personal communication.

able that these operations may also arrest efferent (? antidromic) discharges from the brain stem and thus break the vicious circle of reverberating excitation. A discussion of the surgical therapy would be incomplete without analyzing the Taarnhøj operation. The term "decompression" is inappropriate for this procedure. Many neurosurgeons (Shelden,[29] Hamby,[30] and others) believe that the favorable effect of Taarnhøj's operation depends on two factors: (1) the unavoidable surgical trauma to the root and the ganglion, which need not be severe enough to cause clinically demonstrable sensory disturbance; (2) possible interference with the blood supply of these structures (Stender[31]). Experimental studies by King and Meagher present here, again, some confirmatory evidence: Cats with aluminum oxide gel injection into the spinal trigeminal nucleus lost their cutaneous overreaction to tactile stimulation and the corresponding central delayed response, after the Gasserian ganglion had been mildly traumatized; the animals showed, however, no gross sensory changes. If one applies observations made in experimental nerve injuries, the large tactile and proprioceptive fibers in the sensory root (which carry the afferent component of the pathologic trigeminal reflex) may be more susceptible to mechanical trauma than the other fibers of the root. The fact that minor surgical trauma to the root fibers or Gasserian ganglion relieves an existing tic douloureux would appear to argue against the idea that true tic douloureux is produced by a mechanically irritative or compressive lesion adjacent to the root or ganglion.

Summary and Conclusion

The literature concerning the pathogenesis of trigeminal neuralgia is reviewed.

So far, no specific morphologic basis has been established for the so-called idiopathic trigeminal neuralgia.

The concept is proposed that the neurodynamic mechanism of the paroxysm of tic douloureux is central and that it represents a pathologic multineuronal reflex in the trigeminal system of the brain stem. Physiologic afferent stimulation (tactile or proprioceptive) of trigeminal, and, occasionally, of high cervical, receptors evokes a pathologically increased delayed response in the spinal trigeminal nucleus; from there, efferent impulses are conducted back to the periphery, where they reverberate and reexcite the central trigeminal connections. This process of self-exciting repetitive after-discharge continues until the firing neurons become refractory.

It is suggested that the abnormal overexcitability may be caused by senescent (metabolic) changes of the ganglion cells of the trigeminal nucleus. Such changes may be possibly modified by pharmacologic substances, such as thiamine and cyanocobalamin (vitamin B_1 and B_{12}).

Morphologic or functional vascular disturbances are contributory, but not primary, factors in the production of the attacks of tic douloureux.

The effect of surgical treatment of tic douloureux depends on successful abolition of the abnormal trigeminal reflex. Not only are the physiologic afferent impulses from the periphery blocked, but also the abnormal central efferent impulses are interrupted by the surgical procedures. The Taarnhøj operation does not act as a mechanical decompression, but eliminates the pathologic trigeminal reflex response by subclinical traumatization of the sensory root and Gasserian ganglion.

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Jean-Martin Charcot (1825-1893)

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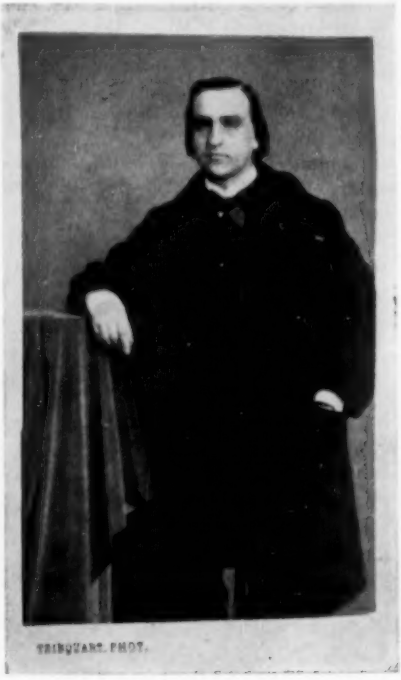
Published a few months ago in *Le Progrès médical* was an article on Charcot by the French historian, Dr. Pierre Astruc,[1] in which Prof. Georges Guillain's long-awaited biography on Charcot [2] was reviewed in some detail. What struck Dr. Astruc as important in Professor Guillain's monograph seems worthy of noting, in a somewhat modified form, in English.

Thanks to Professor Guillain for settling the point, the admirers of Charcot need not trouble themselves to search for his birthplace in Paris, 1 rue du Faubourg Poissonnière, for it has been demolished. The four Charcot sons, of whom Jean-Martin was the second, were brought up here. In his late teens, Jean-Martin wavered in his choice between medicine and art, then decided on a medical career. Although not in financial straits—for his father was an accomplished carriage maker—Jean-Martin had to live modestly while a medical student. His taciturn character was somewhat out of keeping with the demeanor of dandy which he adopted. He had a John Barrymore profile, of which he made innumerable sketches from his 20th year onward. Like his friend Lasègue, he became a first-rate caricaturist, and he devoted many a night to painting on china and enamel.

In 1848 Charcot was promoted to *résidant de l'hôpital* (hospital resident), along with Axenfeld, Potain, Trélat, and Vulpian. His residency was under Rayer. Five years later his thesis was accepted. He became *médecin des hôpitaux* in 1856, and *agrégé* in 1857, along with Marcé, Potain, Lorain, Vulpian, Parrot, and Laboulbène. When, in 1862, he was appointed *médecin* to the Salpêtrière, his attention turned to neurology. In 1872, when Vulpian vacated the chair of pathological anatomy to accept another in experimental pathology, Charcot was his successor. He taught pathological anatomy and continued to sharpen his acumen in clinical neurology: These activities led him straight to the chair of clinical neurology, created in 1882, at the Faculty of Medicine in Paris, the first in the world. "His name," wrote Vulpian, "is as well known abroad as to the people of France, and, if the world accords France first place in the study of pathology of the nervous system, as seems to be the case, this is due incontestably to the discoveries of M. Charcot." He was elected

Fig. 1.—Jean-Martin Charcot at approximately 47 years. Courtesy of Dr. Maurice Genty, Paris.



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to the Academy of Medicine in 1872. Eleven years later on his election to the Academy of Sciences, he pronounced these words: "I believe that medical practice has no real autonomy, that it lives by borrowing, by application; that without incessant scientific renewal it becomes an obsolete routine."

Throughout his life, Charcot was always watchful for progress, working without surcease, and stimulating his pupils to produce a maximum of scientific output. As a renowned consultant, he traveled from capital to capital. But his fast pace led to its logical outcome on August 16, 1893, when he was 68. The nature of that catastrophe has been enshrouded by the diagnosis "acute edema of the lungs." It all happened in the Hôtel du Lac des Settons in Morvan, where he was in the company of his old pupils, Straus and Debove. Professor Guillain relates this dramatic event, quoting an eyewitness to the early part of the journey, René Vallery-Radot: On setting out from Paris, the party was in high spirits, the conversation never languishing for lack of witticisms. The travelers visited the Château de Bussy, the basilica of Vézelay (austere as a citadel or a prison, said Charcot), Pierre-Perthuis, and the river Cure, and, the following day, in Morvan, after some further excursions, enlivened by philosophical and religious recollections and climaxed by a jovial dinner, the inevitable occurred.

Aided by close associates of Charcot, Professor Guillain recreates the personal characteristics of the master. Although outwardly impassive and cold, he was, asserts Professor Debove, inwardly emotional and tense. One had to know him very well to perceive the tear that readily pearled on the border of his eyelid when confronted with an emotional situation. On evenings out he could be the life and soul of a gathering, but he preferred to remain at home, where he was a bit somber. He would, however, relax at the table to feed his favorite monkey or dog. He was a regular visitor to museums, an ardent listener to music, an omnivorous reader. He kept aloof from politics, but enjoyed the company of Gambetta.

From the international point of view, Charcot's sympathies were closest to England. He scoffed at the nationalism of Virchow in these terms:

> The nonliberal ideas of the Prussian sage can be contrasted with the magnificent words of one of England's great physicians: "Reason," said Graves, "has extended its empire from the old to the new continent, from Europe to the Antipodes; today her domain is the entire world, on which the sun never sets. Individuals sleep, but the collective intelligence of the species never sleeps."

Quite another Charcot was the physician who received his patients in the long library, darkened by stained-glass windows, at 217 boulevard Saint-Germain; still another, the brilliant host to scientists, physicians, artists, and politicians—among the latter, Waldeck-Rousseau, the son-in-law of Madame Charcot, previously Madame Durvis. Professor Guillain deals at length with the Charcot of the Salpêtrière, where, in that medical temple which was his office—an old room of *l'ancienne Pharmacie*, which had once been a kitchen—Charcot examined his patients. It was here, too, that Charcot lectured to his staff. The clinic amphitheater was the scene of gatherings of quite a different kind, with physicians from all corners of the earth in attendance. "The Friday formal weekly lecture was the great affair of a lifetime," said Pierre Marie. Tuesday's lectures were improvised and consisted, as a rule, of a running commentary on some one subject, such as pathological gait, which he demonstrated in the groups of patients which were led before him.

Among the French and the foreign doctors who attended his lectures were many who were to become future professors of the Faculté de Paris: Bouchard, Cornil, Joffroy, Debove, Straus, Hanot, Raymond, Brissaud, G. Ballet, and Pierre Marie. Others became illustrious in the French provinces: R. Lépine and Pierret, at Lyon; Duret, at Lille; Pitres, at Bordeaux. All the élite in French neurology were drawn from the apron of Charcot: Babinski, Ball, Bourneville, Dutil, Féré, Gombault, G. Guinon, Hallion, Meige, Parmentier, Souques, Gilles de la Tourette.

Among those hailing from other countries were Bechterew and Marinesco. Another was Freud, who wrote that Charcot's fame "will always be above opinions and time." Not all his pupils remained devotees. Professor Guillain has given the reasons for the rupture with Bouchard. This episode, which brought a tardy repentance from Bouchard at Debove's prodding, was exceedingly painful to Charcot, whose deference for his pupils was such that in competitive examinations he overlooked rhetorical combats and judged only by the scientific work they had accomplished. Charcot crossed swords also with Brown-Séquard over the problem of localization in Jacksonian epilepsy.

When Charcot appeared on the scene in about 1850, the pickings in pathology were still very lean. Among the classical works, wrote Professor Guillain, one finds a little which is enlightening on hemorrhage and softening of the brain, encephaly, hydrocephaly, atrophy and hypertrophy of the brain, and tumors. On spinal cord disorders there existed vague descriptions of malformations, contusions and other wounds, congestion and apoplexy, myelitis, atrophy, and hypertrophy. Epilepsy, chorea, and tetanus were regarded as neuroses. By the time Charcot died, the modern outline of disorders of the nervous system had taken shape.

Charcot contributed not a little to this development. His description, in 1853, of the clinical forms of chronic progressive rheumatism has remained a classic. Ten years later, with Cornil, he studied the kidneys and joints of the gouty. In this field, Garrod paid him homage. In geriatrics he was a precursor, and he protested against the *littérateurs* who represented all old men as trembling from head to foot. To him we owe the first description of intermittent claudication, studies on painful paralysis in metastatic cancer, and an explanation of the pathogenesis of cerebral hemorrhage, which has somehow become associated with Bouchard's name.

It was Charcot who recognized the ominous prognosis of gluteal decubitus of rapid onset, the meaning of ophthalmic goiter, which he made known in France, and the difference between Parkinson's disease and multiple sclerosis. He was the first clearly to delineate the principles of cerebral and spinal localization of lesions. "Orderliness and logic are very closely related," Bossuet wrote, and the works of Charcot are as remarkable for the one as for the other.

His work on amyotrophic lateral sclerosis, of epic proportions, was done under the influence of Duchenne, "his teacher in neurology" Charcot liked to say of him. His discussion of the tabetic arthropathies in London, in 1881, aroused the enthusiasm of Paget. In aphasia he did much to shake the doctrine established by Broca. Animal research was not one of his interests; Over the door of one of his laboratories he had inscribed, *"Vous ne trouvez pas une clinique de chiens chez moi."*

Professor Guillain protests against the oblivion into which Charcot's work on hysteria has fallen. "History judges a medical or scientific work relative to the time at which it was created." Charcot did not have available the modern means by which simulation can be unmasked. Nevertheless, he had the acumen to distinguish hysteric from epileptic convulsions and to reject the hysteroepilepsy concept. According to him, "one encounters simulation at each step in hysteria; and at times the physician is surprised at the gratification he himself obtains in seeing through the ruse and in detecting the extraordinary sagacity and tenacity with which the simulation is perpetrated, above all when the victim of the imposture is a physician."

It was against this psychological background that Charcot saw the stigmata of hysteria. Not only did he recognize the significance of simulation, but he also envisaged the role in the production of hysterical phenomena of "emotion, imagination, suggestion, confabulation and falsehood." On the participation of these several fac-

tors, states Professor Guillain, there is general agreement.

It is interesting to note that in the German-speaking and Slav countries in Europe the merits of Charcot as one of the founders of the concept of functional psychical disturbances have never been questioned. Further, these countries never participated in the dispute which, in some aspects, was a purely domestic French affair. As a matter of fact, the concept of Babinski that the manifestations of hysteria are the product of suggestion was too narrow and therefore found no support in the countries outside France. Also, the term pithiatism (πειθώ=persuasion; ἰατός=curable) proposed by Babinski as a better name for hysteria, never acquired popularity in the other countries of Europe. Although most psychiatrists nowadays hold reservations on Charcot's concept of the *grandes crises nerveuses*, they fully accept the reality of his *crises mineures*. The present-day tendency to emphasize the constitutional factor, the so-called "hysterical character," may be regarded as a further development of the fundamental concept promulgated by Charcot with respect not only to hysteria but also to the neuroses. There is no denying that Charcot laid the foundation of psychopathology on which Janet and Freud, both his pupils, built so well.

Charcot was interested in hypnotism but, remarked Professor Guillain, "he never personally hypnotized a single patient, never supervised a seance and, consequently, was not in a position to evaluate the procedure." His last article, "La foi qui guerit" ("Faith Healing"), appeared in the *Nouvelle iconographie* and in the *Revue hebdomadaire*; he insists there—one last time—on the mental state eminently favorable to faith healing, and agreed with Shakespeare that "there are more things in heaven and earth than are dreamt of in your philosophy."

The biography provided by Professor Guillain is the only complete one that has appeared on Charcot. Woven into the story are the contributions of Charcot's pupils. We find also an account of Charcot's son, Jean Baptiste, the intrepid polar explorer, who led the search for the lost Amundsen. Scattered through the book are illustrations of the Salpêtrière, of Charcot the resident, of Charcot in official gown, of the Charcot medal engraved by Vernon, and of the

Fig. 2.—Monument to Charcot at Lamalou-les-Bains, Hérault, as it appeared before the German Occupation of France. It was dedicated in 1902, nine years after the death of Charcot. Reproduction by permission of Pierre Petit (Yvon), Paris.

bronze by Falguière, which was removed by force from the entrance of the Salpêtrière by the Germans in 1942 and sent by them to the smelter. Alas! The other statues of Charcot had no better luck. At the end of 1943, the bust sculptured by Mme. Charcot, which had been placed on the graceful monument that adorns l'avenue Charcot at Lamalou-les-Bains, Hérault, met a like fate. That bust surmounted a fountain. The abundant foliage of the trees of the adjacent casino protected Charcot's head from the ardor of the sun. On both sides of the now decapitated pedestal, bas-reliefs form a semicircle: on the right, Charcot watches an hysterical woman in a crisis; on the left, two attendants support a tabetic, whom they lead toward a swimming pool. A small jet of water falls into an

alabaster vase and from there, drop by drop, into a basin under whose floating leaves some little goldfish make their untiring round.

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1. Astruc, P.: Charcot, Prog. méd. 83:292-293, 1955.

2. Guillain, G.: J.-M. Charcot, 1825-1893, sa vie—son œuvre, Paris, Masson & Cie, 1955.

Abstracts from Current Literature

Edited by Dr. Bernard J. Alpers

Physiology and Biochemistry

MECHANISM OF COPPER DEPOSITION IN THE LIVER IN HEPATOLENTICULAR DEGENERATION (WILSON'S DISEASE), L. L. UZMAN, F. L. IBER, T. C. CHALMERS, and M. KNOWLTON, Am. J. M. Sc. 231:511 (May) 1956.

These studies were undertaken to ascertain the relative affinity of normal liver and of the liver in Wilson's disease for ionic copper. Liver tissue was obtained from two normal subjects and from one with asymptomatic hepatolenticular degeneration. At a concentration of 8 per milliliter, the abnormal liver had bound five times as much copper as the normal liver. This avidity for copper was attributable to nondialyzable protein or polypeptide fraction.

BERLIN, New York.

THE CEREBRAL PHYSIOLOGIC CONTROL OF HYPOTENSION. J. F. FAZEKAS, S. N. ALBERT, and R. W. ALMAN, A. M.A. Arch. Surg. 73:59 (July) 1956.

The cerebral hemodynamics and metabolism of 21, mostly hypertensive, patients were studied under hypotensive anesthesia induced by trimethaphan camphorsulfonate (Arfonad). In sever induced hypotension the compensatory activity of cerbral vessels is overcome and, consequently, the cerebral blood flow reduced to dangerously low levels. If, however, induced hypotension is only moderate and prolonged, a normal cerebral blood flow is established by a compensatory vascular dilatation in spite of the lowered sytemic blood pressure. Arteriosclerotic and/or hypertensive patients do not tolerate hypotensive anesthesia as well as normal persons because their compensatory cerebral vascular mechanism is less effective. Controlled moderate hypotension is safe for the patient but does not seem to improve hemostasis in brain operations.

LIST, Grand Rapids, Mich.

NYSTAGMUS AS A PHYSICAL SIGN IN ALCOHOLIC INTOXICATION. D. E. HOWELLS, Brit. M. J. 1:1405 (June 16) 1956.

Howells conducted experiments of 12 volunteer medical students to obtain additional information regarding nystagmus as a sign of alcoholic intoxication. He gave ethyl alcohol to determine the approximate amount of alcohol needed to produce nystagmus. In addition, he measured the reaction time before imbibition of alcohol and after the onset of nystagmus, and, finally, he substituted whisky or gin for ethyl alcohol to determine whether the result differed from that produced by the ethyl alcohol.

In all subjects nystagmus developed after varying periods following imbibition of from 0.7 to 1.4 ml. of alcohol per kilogram of body weight. In every case the appearance of nystagmus was accompanied by an increase in reaction time. Whisky or gin produced the same effects.

ECHOLS, New Orleans.

ELECTROENCEPHALOGRAPHIC INVESTIGATION OF THE EXPERIMENTAL CONVULSIVE SEIZURE. A. KRIENDLER, V. VOICULESCO, R. BROSTEANU, I. VOINESCO, and V. NESTRANU, Rev. neurol. 94:120, 1956.

The cortical and subcortical electrical activity was recorded during and after a seizure induced in cats by electroshock and by injection of aminopyrine N. F. (Pyramidon). During the tonic-clonic phase the waves recorded from the thalamus, hypothalamus, and cortex were synchronized, but the amplitude was lower in the subcortical structures. This synchronization of similar wave furrows disappeared at the termination of the seizure, to be replaced by comb-teeth type of 16-21-cps waves of 100μv-150μv in the subcortical structures, such as the thalamus, fimbria fornicis, and corpus callosum. Also, unilateral and bilateral lesions of the centromedian nucleus of the thalamus and hypothalamus appeared to prolong the seizure. The onset of the electrical activity indicating a seizure may precede the actual seizure, and the

electrical disturbance may occur in cortical or subcortical structures. As the seizure develops, there is synchronization of the cortical and subcortical activity, but lesions of the thalamus tend to reduce this synchronization. It is inferred that seizures represent a synchronization of cortical and subcortical activity, but that the thalamus aids in the desynchronization, and hence arrest of the seizure.

BERLIN, New York.

Neuropathology

HEPATIC DUCT CARCINOMA 17 YEARS AFTER INJECTION OF THORIUM DIOXIDE. J. C. ROBERTS JR. and K. E. CARLSON, A. M. A. Arch. Path. 62:1, 1956.

Roberts and Carlson report the case of a woman who died at the age of 45 of carcinoma of the hepatic duct with metastases to the regional lymph nodes, porta hepatis, spleen, lungs, bone marrow, and adrenal glands. Seventeen years previously a colloidal suspension of thorium dioxide (Thorotrast) had been injected to demonstrate arteriovenous fistulas in her right leg. The exact amount of contrast medium employed was not known. Prior to death, roentgenograms had disclosed opaque areas in and near the spleen, which were interpreted as representing deposits of Thorotrast. The amount of residual thorium dioxide was determined in wet pieces of lymph node, liver, and spleen. Radioactivity (counts per minute) per gram of tissue was greatest in the lymph node; total radioactivity (per weight of organ in grams) was highest in the liver. Autoradiographs disclosed alpha tracks corresponding to the granular purple-brown refractile material seen in routine sections stained with hematoxylin and eosin.

APONTE, Philadelphia.

DEATHS FOLLOWING ELECTROTHERAPY. S. P. ALEXANDER, L. H. GAHAGAN, and W. H. LEWIS JR., J. A. M. A. 161:577 (June 16) 1956.

Deaths associated with electroconvulsive therapy given in a state hospital occurred in five instances out of a series of about 70,000 treatments given to 5325 patients. The deceased patients were three men and two women, and their ages ranged from 38 to 57 years.

Autopsies, obtained in four of the five cases, yielded evidence of coronary artery disease that had not been clinically evident. These deaths were not predicted or predictable.

The fatality rate is low (one death per 1000 patients treated), and the figures express the inherent risk of treatment. But the inherent risk of treatment cannot at present be eliminated, largely because of the presence of undetected coronary artery sclerosis and its effect upon the cardiovascular responses to electric stimulation. Despite these complications, whenever treatment is indicated, this fact should, as a rule, outweigh other considerations. However, the possibility of alleviating the cardiovascular strain of this treatment by the use of oxygen, of various drugs, and of various other modifications of the technique should receive attention.

ALPERS, Philadelphia.

AN EVALUATION OF GLIOMAS DERIVED FROM THE EPENDYMAL ANLAGE. N. MUKAI, J. Neuropath. & Exper. Neurol. 15:33 (Jan.) 1956.

Mukai draws attention to the multiple intrinsic habits of neoplastic ependymal cells. The blastomatous type of ependymoma constitutes a divergent type of cellular morphology, in association with the bizarre megalocytic component and certain perivascular patterns of alignment.

Comment is made concerning the intimate relation between the anaplastic form of ependymomas and pineal tumors.

Mukai observed a great similarity in the morphology of subependymomas and that of certain ontogenetic cells; the presence of immature glial cells of ependymal anlage, as well as fibrillary astroglia, was observed. From studies of lithium carbonate stains, he believes that these subependymomas should be classified under ependymomas rather than cerebellar astrocytomas.

SIEKERT, Rochester, Minn.

SPINAL GANGLIONEUROMA. W. B. SCEDCILLE, J. L. POLCYN, and R. H. DUNSMORE, J. Neuropath. & Exper. Neurol. 15:85 (Jan.) 1956.

Six cases of the uncommon intraspinal ganglioneuroma are reported, the tumor in five being of dumbbell configuration. Two cases were asymptomatic; the other four had evidence

of intraspinal pressure. Enlargement of intervertebral foramina, alteration in cerebrospinal fluid dynamics at lumbar puncture, elevated protein content in the spinal fluid, and appropriate defects on myelography were observed. Microscopically, three were unequivocally cases of ganglioneuromas; in two others there existed the possibility of neurofibromas with enmeshed ganglion cells; in the remaining, a myxofibroma with enmeshed ganglion cells. All tumors appeared benign and slow-growing. The surgical treatment has resulted in neurologic cure, with no recurrence in a two- to seven-year follow-up.

SIEKERT, Rochester, Minn.

TRANSNEURONAL CHANGES IN THE INFERIOR OLIVE AND PONTINE NUCLEI IN KITTENS. A. TORVIK, J. Neuropath. & Exper. Neurol. 15:119 (April) 1956.

Torvik describes transneuronal changes in portions of the inferior olives bilaterally after mesencephalic and thalamic hemisections, confined to those areas receiving descending afferents, and in the homolateral pontine nuclei after unilateral cortical or cerebral peduncle lesions. The majority of the neurons showed shrinkage and karyorrhexis and early affection of the nucleolus—a few nerve cells exhibited chromatolysis. The early changes are seen three to four days after the lesion. These changes differed microscopically from retrograde degeneration. Also, the microglial reaction was intense, with only very slight astroglial response.

It is suggested that transneuronal degeneration involves disturbances in cellular metabolism.

SIEKERT, Rochester, Minn.

CEREBRAL INFARCTION PRODUCED BY VENOUS DISTENTION. D. DENNY-BROWN, S. HORENSTEIN, and H. C. H. FANG, J. Neuropath. & Exper. Neurol. 15:146 (April) 1956.

Denny-Brown, Horenstein, and Fang produced complete ischemia and subsequent necrosis of cerebral tissue by distending a vein suddenly with the retrograde injection of saline at a pressure of approximately 50 mm. of mercury. This is termed "retrograde ischemia." As the injection was made, the blood was washed out of the vein; then, with increasing pressure, the area drained by the injected vein blanched suddenly. The injection was then stopped. The pallor remained for 30 seconds and was sharply circumscribed. It is concluded that the pallor is the consequence of arteriolar spasm induced by distention of the arterioles by back-pressure transmitted through the capillary plexus.

Restitution of the circulation was partial, followed by complete stasis and subsequent necrosis. Polarographic recordings showed immediate anoxia. After the first hour there was diffusion of oxygen from neighboring areas.

Refilling of the blood vessels was associated with sludging of the erythrocytes and transudation of plasma through the damaged endothelium. The nerve tissue showed progressive deterioration, beginning as early as one hour. The primary change was damage to the vascular endothelium. Polymorphonuclear cells began to appear on the second day and disappeared after the sixth. Macrophages began to appear in large numbers at the periphery of the infarct on the third and fourth days, multiplying on the outer surfaces of capillary loops. They progressively eroded the infarct. In the material studied the compound granular corpuscle was derived from mononuclear cells (blood-borne) in the lumen of new capillaries. Phagocytic activity resulting from the microglia present in the tissue subsequently infarcted was ineffective; invasion of microglia from adjacent and unaffected tissue was not observed; proliferation of lymphocytic cells in the perivascular spaces was minimal. The sprouting of new capillaries in the most superficial layer of the infarct was the essential process in the formation of the fat-granule-cell layer.

SIEKERT, Rochester, Minn.

PERINEURONAL SATELLITE CELLS IN THE MOTOR CORTEX OF AGING BRAINS. R. H. BROWNSON, J. Neuropath. & Exper. Neurol. 15:190 (April) 1956.

Brownson concludes that the ratio of perineuronal satellite cells, i. e., the astrocytes and oligodendroglia and microglia cells lying around the giant pyramidal motor neurons, is not altered with age.

SIEKERT, Rochester, Minn.

Psychiatry and Psychopathology

NEUROPSYCHIATRIC SEQUELAE OF PREMATURITY. H. KNOBLOCH, R. RIDER, P. HARPER, and B. PASAMANICK, J. A. M. A. 161:581 (June 16) 1956.

The physical and mental status of 992 infants was studied with the help of the Gesell developmental examination and a physical examination, so as to compare 500 single-born premature infants with 492 infants born at term. The comparison was made at age 40 weeks for the full-term infants and at the corresponding corrected age for the premature infants. The two groups were matched as to race, socioeconomic status, and other significant factors.

The incidence of abnormalities was found to increase as the birth weight group of the infant decreased, so that 50.9% of the infants with a birth weight less than 1.501 gm. had defects ranging from minor neurological damage to severe intellectual deficiency. Some of these also had major visual handicaps.

The adjusted percentage of premature infants who showed some departure from normal development was 25.7%, as compared with 12.8% of the full-term controls.

ALPERS, Philadelphia.

Meninges and Blood Vessels

COMPLICATIONS OF MENINGOCOCCUS INFECTION IN A SERIES OF 63 CONSECUTIVE SPORADIC CASES. J. L. TOBIN, Am. J. M. Sc. 231:241 (March) 1956.

In a four-year period, 63 sporadic cases of meningococcic meningitis were observed, occurring in every season. There was never more than one case at a time in a group of 72 persons who worked and lived together, presumably because of administration of sulfadiazine to all members of the group in which the case of meningitis occurred. Complications of meningitis occurred in 50.8% of those afflicted. The commonest complications were the Waterhouse-Friderichsen syndrome, neural effects, such as cranial nerve palsies and herpes zoster, and ulceration of the skin. Cortisone was ineffective in cases of adrenal insufficiency, but arterenol (norepinephrine) was effective in transiently sustaining the blood pressure.

BERLIN, New York.

Diseases of the Brain

ORGANIC BEHAVIOR DISORDER: BEHAVIOR CHARACTERISTICS OF BRAIN-DAMAGED CHILDREN. D. H. MILMAN, A. M. A. J. Dis. Child. 91:521 (June) 1956.

Milman reaffirms the thesis that minimal degrees of brain damage produce the distinctive clinical features of motor incoordination, perceptual difficulties, social ineptness, anxiety, disabilities in speech and reading, and failure in school. The personality reacts to the consequences of repeated failure in mastering motor skills, etc., by anxiety, depression, negativism, aggression, and retreat to a less mature level. An interpretation should be given to the parents on the nature of the disability and the areas where help is needed.

SIEKERT, Rochester, Min.

Diseases of the Spinal Cord

BROWN-SEQUARD SYNDROME WITH BILATERAL ELEPHANTIASIS IN NEUROFIBROMATOSIS. L. H. HUDSON and T. R. COX, J. A. M. A. 161:326 (May 26) 1956.

Hudson and Cox describe a patient with neurofibromatosis complicated by bilateral upper extremity elephantiasis and a Brown-Séquard type of hemiplegia with ipsilateral diminution of pain and temperature response. This case, in addition, demonstrates the ability of an apparently long-standing cervical deformity to produce a sudden hemiplegia.

Neurofibromas have been described in association with neural tissue throughout the body. In elephantiasis there is marked overgrowth of the neural sheath tissue with disruption of the peripheral nerves and blockage of the venous and lymph channels. In the case reported here, the marked tumor overgrowth encroached upon the vascular channels, so that the lymphatic dilatation could be explained by mechanical blockage. Trauma to the right arm was followed by increased size.

The right arm was amputated because it was functionally useless and its weight a hindrance to the patient. Removal of the redundant tissue from the left arm greatly enhanced its motility.

Up to 43% of patients with generalized neurofibromatosis have scoliosis and kyphosis. The lower thoracic and cervical vertebrae are commonly involved. A severe gibbus may give symptoms of compression on the spinal cord. A gibbus deformity usually develops slowly, but there may be a history of sudden exacerbation of symptoms. In 20 cases of paraplegia with neurofibromatosis, 60% were due to extreme gibbus deformity. In two of four cases of Brown-Séquard syndrome reported by J. C. Christensen, the patient was relieved of symptoms by correction of a herniation of the nucleus pulposus at the point of flexion deformity. The sudden onset of symptoms in the case here reported might have been due to such a sudden herniation. Surgical exploration for herniation of the nucleus pulposus and neurofibroma in the cervical canal was probably indicated.

ALPERS, Philadelphia.

Peripheral and Cranial Nerves

POSTURE AND CERVICOBRACHIAL PAIN SYNDROMES. D. A. JOHNSON, J. A. M. A. 159:1507 (Dec. 17) 1955.

The common factor in a variety of cervicobrachial syndromes is posture. In an effort to develop a more practicable clinical approach to the problem of cervicobrachial pain and paresthesias, the author defines a diagnostic category based on the factor common to so many cervicobrachial syndromes, i. e., the postural factor. Postural myoneuralgia is a descriptive term for this category.

The diagnosis of a postural disorder rests on (1) a characteristic history, (2) shoulder-girdle tilt, (3) all or some part of the characteristic pattern of muscle tenderness to point pressure, and (4) a bruit over the subclavian artery when the arm is abducted. One or more of these elements is often lacking, and none is specific.

Johnson feels that the concept presented here will simplify the diagnosis of this type of disorder, improve the selection of patients in whom surgical intervention may be indicated, and provide effective and simple treatment for some patients who would otherwise be treated inappropriately or be relegated to a diagnostic category that implies no effective treatment is available. He outlines a simple exercise program for treatment.

ALPERS, Philadelphia.

Treatment, Neurosurgery

GLOSSOPHARYNGEAL BREATHING AS AN AID TO RECOVERY FROM PARALYTIC POLIOMYELITIS. W. D. LOESER, Am. J. M. Sc. 231:487 (May) 1956.

Glossopharyngeal breathing was used in the rehabilitation of four patients with respiratory paralysis. The process consists of forcing the air toward the larynx by the mouth, tongue, soft palate, and pharynx. After the gulping effort, the larynx is closed. When the vocal cords are opened, passive exhalation occurs. This technique permitted these patients to have a prolonged unassisted breathing time, increased vital capacity, forced cough, and mobility of the chest cage. It may provide a rest for fatigued respiratory muscle.

BERLIN, New York.

THE TREATMENT OF TUBERCULOUS MENINGITIS WITHOUT INJECTIONS. W. P. SWEETNAM and C. G. W. SYKES, A. M. A. J. Dis. Child. 92:2 (July) 1956.

In a small group of children with tuberculous meningitis isoniazid alone was as efficacious as a combination of isoniazid, aminosalicylic acid, and streptomycin.

SIEKERT, Rochester, Minn.

TREATMENT OF DELIRIUM TREMENS WITH RESERPINE (SERPASIL). M. AVOL and P. J. VOGEL, J. A. M. A. 159:1516 (Dec. 17) 1955.

Twenty-three patients were treated with reserpine (Serpasil) in an attempt to control the symptoms of delirium tremens. The drug was given parenterally in relatively large doses,

ranging from 2.5 to 5 mg. in one injection. The patients were free of their symptoms of acute hallucinations in an average of 18 hours. Most of the patients were free of their symptoms within 24 hours. The shortest period of time noted was 9 hours (two patients), and the longest was 48 hours (two patients).

Despite the relatively large doses utilized, there were no ill-effects noted in this series. Hypertensive cardiovascular disease per se is not a contraindication of the use of the drug, although the drug should be used with great caution in these instances. Because of the great variations in reaction to this drug, the dose should be individualized. Avol and Vogel have found that an initial dose of 2.5 mg., to be followed in three hours by another dose of 2.5 mg. if necessary, is fairly safe for all patients.

The use of this drug has greatly shortened the time necessary to free these patients of their postalcoholic withdrawal symptoms. Moreover, they are a much easier group to care for from the point of view of nursing.

ALPERS, Philadelphia.

SURGICAL ALLEVIATION OF PARKINSONISM. I. S. COOPER, N. POLOUKHINE, and A. MORELLO, J. A. M. A. 160:1444 (April 28) 1956.

This report summarizes the current status of an investigation of two new neurosurgical techniques used in the treatment of far-advanced Parkinsonism. These techniques are surgical occlusion of the anterior choroidal artery, which has now been used as an investigative technique for two and one-half years in a series of 50 cases, and chemopallidectomy (used in 125 cases), which consists of nonstereotactic injection of either anesthetic or neurolytic agents into the region of the globus pallidus, with use of a pneumoencephalogram to aid in orientation of the cannula.

It is not the purpose of this report to suggest that either or both surgical occlusion of the anterior choroidal artery or chemopallidectomy should necessarily become a standard procedure in the treatment of Parkinsonism. However, it has been demonstrated that even the patients with the most far-advanced cases and those who are most disabled have conditions potentially amenable to surgical therapy. It has also been shown that relief of rigidity, tremor, and deformity can be achieved without sacrificing motor power.

The authors conclude that further efforts are justified to improve these and other surgical techniques aimed at the mesial globus pallidus, to improve methods in the selection of patients, and to lessen the risks of operation. The possible avenues of approach seem clear-cut, and, as in lobotomy, many variations of technique will doubtlessly be possible. It is anticipated not only that improved surgical therapy will ensue during the further development of these techniques, but also that some contribution will be made to an improved understanding of the pathological physiology of hyperkinetic disease.

Good results were obtained in 70% of patients treated with chemopallidectomy. The follow-up of the early successful cases of occlusion of the anterior choroidal artery and chemopallidectomy demonstrated that the good results are enduring.

ALPERS, Philadelphia.

FIVE-YEAR FOLLOW-UP OF PATIENTS SUBJECTED TO THREE DIFFERENT LOBOTOMY PROCEDURES. N. L. PAUL, E. FITZGERALD, and M. GREENBLATT, J. A. M. A. 161:815 (June 30) 1956.

A five-year follow-up of 116 chronically mentally ill patients, divided into three groups, each of which was subjected to a different type of lobotomy (full bilateral, bimedial, and unilateral), disclosed that bimedial lobotomy is superior to either of the other two procedures in the treatment of chronically mentally ill patients.

Thirty-four per cent of the patients who had had a bimedial lobotomy showed marked improvement at the end of five years, as compared with 18% of those who had had a bilateral and 14% of those who had had a unilateral lobotomy. Patients in all groups showed improvement in work adjustment at the five-year follow-up over that observed at the one-year follow-up; this was particularly true in the patients who had had a bimedial lobotomy, 54% of whom had a good work adjustment after five years, as compared with 33% of those who had had a bilateral and 29% of those who had had a unilateral lobotomy. The number of patients who had had one or more convulsive seizures was greater after five years than after two years; only one person, however, had status epilepticus caused by the operation, and this proved fatal.

The five-year follow-up shows the superiority of the bimedial lobotomy in the treatment of chronically mentally ill patients. It is therefore strongly suggested by the authors that the bimedial lobotomy be used in preference to either the full bilateral or the unilateral procedure.

ALPERS, Philadelphia.

GUANIDINE AND MYASTHENIA GRAVIS. M. J.-E. DESMEDT, Rev. neurol. 94:154, 1956.

Eight patients with myasthenia gravis received 15 to 35 mg. per kilogram of guanidine hydrochloride by mouth. In seven of these the effect on motor performance was comparable to that observed after the injection of 1.5 to 3 mg. of neostigmine sulfate. Side-reactions to excessive amounts of guanidine consisted of excitement, vertigo, and paresthesias. The maximal effect of guanidine persisted for six hours, which is longer than that of pyridostigmine (Mestinon). Observations on the effect of the reaction of the adductor of the thumb to stimulation of the ulnar nerve revealed that guanidine reduced the depression of neuromuscular activity from low-frequency, i. e., 1/sec. to 50/sec., stimulation but did not modify the tetanizing effects of 100-400 cps stimulation. There was increased amplitude of muscle response to single shocks. There was no comparable change in normal subjects given guanidine or in those myasthenic subjects who had no weakness. It is postulated that guanidine lowers the threshold of excitation of a group of fibers previously unresponsive to maximal stimulation by sensitizing the motor end-plates to acetylcholine.

BERLIN, New York.

News and Comment

ANNOUNCEMENTS

Chicago Neurological Society.—The newly elected officers of the Chicago Neurological Society for the coming year are Dr. Irving C. Sherman, president; Dr. Ernst Haase, vice-president; Dr. Adrien Verbrugghen, councilor, and Dr. Oscar Sugar, secretary.

Books

BOOK REVIEWS

Etude radio-anatomique de l'os temporal. By M. Juster and H. Fischgold. Price, $5.50. Pp. 101. Masson & Cie, 120 boulevard Saint-Germain, Paris 6°, 1955.

A well-printed and illustrated radiographic atlas of the temporal bone, this volume should be of value to anyone dealing with the intracacies of temporal bone anatomy as seen in the usual x-ray study. Although the text is in French, the authors have included a French-Latin glossary of all the anatomical names, from which transposition into English is quite easy. All x-ray studies are done on the disarticulated temporal bone, so that there are no x-ray plates showing its relations to other portions of the skull. The book is primarily of value for reference and would be of help in neurological and radiological libraries.

Recent Advances in Neurology and Neuropsychiatry. Edition 6. By Sir Walter Russell Brain and E. B. Strauss. Price, $7.50. Pp. 311. Little, Brown & Company, 34 Beacon St., Boston 6, 1955.

For the nine-year interim since the last edition of this book, the authors have attempted to review a great mass of literature in a rapidly expanding field. The result is an excellent summary presentation of the most pertinent advances in neurophysiology, clinical neurology, and neuroradiology. A third of the book is devoted to correlating neurophysiology and the problems of clinical neurology. An excellent review of electroencephalography, by Dr. Denis Hill, will be helpful, informative, and of considerable interest to those whose activities are in other neurological fields. Dr. Hill not only outlines clearly the basic electrophysiology of brain potentials but also deals fully with the clinical significance and application of electroencephalography. For the first time, a section on neuroradiology has been presented in this volume. This not only includes helpful comments on the interpretation of plane skull x-ray films but also describes the techniques of pneumography, angiography, myelography, and positive contrast ventriculography.

There are brief sections on a wide variety of clinical entities with discussions of etiology, symptoms and signs, and most recent advances in therapy.

The literature reviewed is primarily British; this feature is of value to American readers, who may find it difficult to keep informed on advances in neurology on both sides of the Atlantic.

Biochemistry and the Central Nervous System. By Henry McIlwain. Price, $9.50. Pp. 272. Little, Brown & Company, 34 Beacon St., Boston 16, 1955.

The scope of this new book is broader than the title implies. The basic biochemistry and physiology of the central nervous system are reviewed briefly, with referral to examples of altered function in disease. The chemistry at times is too well digested; however, this is the fault of the reader, not the author. From reading the short passages on a given subject one has an excellent summary of the topic, and a good bibliography allows the reader to go further.

The metabolism and chemical composition of the brain in situ, as well as the metabolism of separated cerebral tissues, are outlined and discussed as related to general metabolic changes in health and disease. Cerebral respiration is discussed in detail. The various energy and metabolic pathways are reviewed and then related to specific changes in the nervous system. The cytochemical and histochemical aspects of the nervous system are recounted first in individual cells and then in the brain as a whole unit. The chemical and enzymatic make-up of the brain during development is included. Specific substances are reviewed in detail, including acetylcholine, adrenaline, and arterenol, sympathin, serotonin, glutamic acid, excitants, and depressants. The final chapter is a provocative discussion of the time-scale pattern of rates of cerebral processes relating the chemical and electrical phenomenon as much as possible consistent with brevity.

This is a useful book for quick reference. The index is excellent, facilitating quick reference; and the bibliography, with separate author index, is quite lengthy, with frequent reference to papers published in the last few years.

Television Therapy

Effectiveness of Closed-Circuit Television as a Medium for Therapy in Treatment of the Mentally Ill

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Closed-circuit television has been introduced into the field of mental hygiene as a medium for the administration of therapy to a mass audience. The present evidence indicates that the use of this type of television may promote the development of new and more effective methods for the treatment of the mentally ill.

Closed-circuit television is so named because the program signal is carried directly from one point to another by cable, as opposed to commercial television, which is broadcast indiscriminately. Thus, closed-circuit television reception is restricted and can be seen by only those for whom it is intended.

This report on closed-circuit television therapy begins by describing the observational studies of the effects of commercial television programs on hospitalized mental patients. These preliminary studies later led to the development of the closed-circuit television therapy program.

In the spring of 1953 five television sets were installed on five different wards at Agnews State Hospital. It became apparent, to those employees most closely associated with the patients, that the maintenance of the wards became easier following the introduction of television, since the patients seemed quieter and more easily managed. It was felt that if this apparent improved behavior change could, by investigation, be clearly related to the introduction of television, possibly a new field of research and treatment would be opened.

A review of literature reported no previous research in this area. Therefore, in 1953 (May-July) a pilot study was conducted which served as a first step in the present investigation. One ward was observed daily for a period of six weeks in order to note the patients' reactions to television programs. Many patients appeared to respond with a broad range of behavior reactions: A number of patients would sit and talk to the television performers, usually the newscasters, for long periods of time; some of these patients were normally uncommunicative to anyone. Other patients would imitate performers, especially dancers.

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The research was conducted at Agnews State Hospital, under the auspices of the Department of Psychology, San Jose State College, San Jose, Calif.; Charles W. Telford, Ph.D., Chairman.

Superintendent and Medical Director of Agnews State Hospital, Department of Mental Hygiene, State of California (Dr. Tucker). Professor of Education and Coordinator of Audio-Visual Services, San Jose State College (Dr. Lewis). Originator and principal investigator for this study; postgraduate student in psychology, San Jose State College, and professional intern at Agnews State Hospital (Mrs. Martin). Co-investigator and electronic specialist for this study; postgraduate student in psychology, San Jose State College, and professional intern at Agnews State Hospital (Mr. Over).

Most of the patients appeared to develop preferences for certain television personalities and looked forward to seeing them each day.

Additional television sets were installed throughout the hospital (20 wards had television by December, 1953), and it became evident that more objective consideration should be given to the effects of television on the patients; thus a second study was undertaken in August, 1953. The patients selected for this second study were 67 chronically ill psychotic women who were confined to a closed ward and had had no access to television during their hospitalization. The behavior patterns and activity levels of the patients were observed and evaluated for a three-month period, from Aug. 8 to Nov. 8, 1953. At this time a television set was installed on the ward, and a second period of observation and evaluation was conducted for a three-month period, from Nov. 8, 1953, to Feb. 8, 1954.

It was concluded from this study that there was an over-all average behavior improvement of 9.32% for the entire group under study.* It was further concluded that the use of television should be encouraged to relieve the tedium of institutional existence. By December, 1954, television sets were installed on all 65 wards of the hospital.

The data from the two previous studies encouraged further investigation in order to determine whether various types of therapy could be given to a large group of mentally ill patients by using the medium of controlled closed-circuit television. Then, to formulate a program for closed-circuit television therapy, two hypotheses were postulated.

Hypothesis 1: Therapy can be administered effectively in a simulated face-to-face situation through the medium of closed-circuit television, giving the impression of individual therapy, while administering to a mass audience.

Hypothesis 2: By means of closed-circuit television, motion pictures dealing with mental hygiene and other educational subjects, film strips, and other suitable materials can be presented as often as desirable to reinforce, by repetition and consistency, the basic principles underlying good mental health. Orientation programs, interpretations of hospital and ward routines, and programs of general education and instruction can also be presented effectively to a mass audience through this medium.

The purpose of the third, and most recent, study, which was started in August, 1954, was (1) to examine and evaluate behavioral changes occurring in patients, by means of psychological tests, prior to and following therapy by closed-circuit television; (2) to obtain clinical evaluations of the patients' condition prior to and following therapy by closed-circuit television, and (3) to evaluate the effectiveness of specific therapies presented by closed-circuit television to a mass audience.

The criteria for improvement were (1) clinical estimates of improvement made by the psychiatrist following therapy via closed-circuit television, (2) psychological estimates of improvement based on tests and/or ratings made before and after therapy via television, and (3) increase in permits for visits out, indefinite leaves, and discharge.

Categories for psychiatric evaluations were as follows: worse, no change, borderline toward slight improvement, slightly improved, much improved, and markedly improved.

Procedure

Subjects.—The subjects for this study were 141 women patients hospitalized at Agnews State Hospital. Of these patients, 66 were designated as the control group, and the remaining 75 patients were designated as the experimental group. These two groups were hospitalized in separate wards.

The basic design for the study was to select patients of a comparable age with similar categories of illness in order that the groups would be as nearly equated as possible. Both groups were classified with few exceptions as chronic schizo-

* Findings were based on group data obtained from the Hospital Adjustment Scale by rating and rerating the group behavior prior to and following commercial television.

phrenics of various types. They were reasonably equated as to age and year of admission, and there was very little difference in their behavior patterns and activity levels.

The hospital medical records revealed diagnoses in 20 categories for the control group and in 16 categories for the experimental group. The four major classifications are shown in Table 1.

TABLE 1.—*Major Diagnostic Categories*

Classification	Control Group	Experimental Group
Schizophrenia	42	58
Psychoses associated with organic dysfunction	11	7
Manic-depressive psychosis	8	4
Involutional psychoses	5	6
Total	66	75

At the time of the study the age range for the control group was from 21-77 years, and for the experimental group 22-72 years. On admission to the hospital the mean age for the control group was 40 years, and for the experimental group 36 years. The mean year of admission to the hospital for the control group was 1947, and for the experimental group, 1946.

The education level attained by these patients at the time of their admission to the hospital indicated that 64% of the control group and 55% of the experimental group had had less than a high school education. Nine of the control group patients (13.64%) were in, or had completed, college at the time of admission, while 16 of the experimental patients (21.33%) were so classified.

Apparatus.—A television studio was set up in a visiting room approximately 9 by 16 feet, located off the corridor leading into the experimental ward. The furniture in the studio consisted of 3 library-type tables, 10 folding chairs, a locked cabinet, and 2 small stand tables. The room was lighted by one outside window and three large banks of Slimline fluorescent lights.

The closed-circuit television chain consisted of a television camera, a Zoomar lens, a wide-angle lens, monitor, control unit, and sufficient coaxial cable to complete the circuit to the ward receiver. All lines (coaxial cables and audio lines) were installed in the walls and ceiling of the ward as a safety precaution. The closed-circuit television equipment used in the project was known as a "KAY LAB Television Camera System," and consisted of a very small camera unit with a larger, separate control unit and a separate monitor. An important advantage noted in the use of equipment with a separate monitor was that both the performer and the cameraman were able to see the monitored image. For many of the patients the ability to see themselves perform served as an added incentive to productive response. Most of the patients who participated were pleased and surprised at how well they appeared on television and welcomed the opportunity to participate in programing. An occasional patient who resented seeing herself, or who became preoccupied with her own image, was easily pacified by the simple expedient of turning the monitor so that it could be seen only by the cameraman.

Audio equipment consisted of a public address amplifier, with microphone and phonotape input leading to a speaker concealed under the television set on the ward. Other equipment used in the experiment consisted of (1) a 16 mm. sound motion picture projector; (2) two tape recorders with tapes; (3) motion picture films;† (4) filmstrips;† (5) beaded motion picture screen; (6) slide and filmstrip projector; (7) three-speed record player and phonograph records; (8) desk and stand microphones, with audio amplifier; (9) magazines (current and popular); (10) art supplies (water colors, crayons, modeling clay, and paper); (11) cosmetics (sample-size lipsticks and powder); (12) writing paper and pencils; (13) typewriter and office supplies.

Method.—Two types of televised therapy programs were used continuously during the study: (1) panel and group therapy sessions and (2) selected motion pictures. Other therapies employed in conjunction with the above were music therapy, art therapy, psychodrama, individual therapy, and question-and-answer programs, all of which were televised to the experimental group by closed-circuit television.

Two hundred seventeen different motion pictures were televised to the experimental group, and observations were made regarding the subject's response to each film.‡ Films were used to stimulate group and panel discussions, for entertainment, and for instruction and education. One or more films were televised before each group or panel discussion period. Art films were shown to stimulate interest in art activities; films dealing with music and other activities pertinent to the study were also shown. Seventy-seven films were re-shown one to four times, at the request of the patients.

Televised panel and group therapy sessions were conducted, with five to six patients and a moderator participating in each discussion. Twenty-five such sessions were held, with 17 patients participating

† All films and filmstrips were on loan from San Jose State College Audio-Visual Center.

‡ Films and filmstrips are available from county school departments, the Department of Public Health, and audiovisual libraries; and films may be obtained on long-term loan or deposit from business, industry, and government agencies.

in 2 to 16 sessions each. Twenty of the sessions were conducted by the ward doctor; one, by the superintendent of nursing services; two, by the clinical director in charge of medical research for the hospital, and two, by members of the San Jose State College faculty (one from the nursing education department and the other from the department of psychology). These programs were conducted each Monday and Friday morning for one hour. The following procedure was employed: At 9 a. m. each Monday and Friday a motion picture was televised to the ward. After the picture, the therapy group would adjourn to the studio and begin their discussion, which was televised to the ward. These entire sessions were tape-recorded for later evaluation.

Six different psychodramas involving various conflict situations were conducted and transmitted to the ward by closed-circuit television during the study, with eight different patients participating. The situations usually involved two patients at a time. A member of the research team would give the setting for the conflict situation, and then the patients would work out their own solutions. Televised informal group discussions usually followed each psychodrama. Individual therapy and question-and-answer programs were utilized intermittently throughout the study and televised to the ward.

Voluntary group art activities were in progress approximately three hours a day, following orientation and stimulation programs telecast from the studio earlier in the day. Art supplies consisted of water colors, individual and stock boxes, brushes, crayons, art paper, paper picture frames, paste, construction paper of various colors, modeling clay, finger paints, and picture binding. These supplies were placed on a large library-type table in the day hall of the experimental ward, where patients could use them at any time.

Music was supplied by more than 300 musical selections. This music was played in the experimental ward via the audio circuit, and to the yard (when patients were taken to the exercise yard) through loud-speakers placed in the studio window. An electric record player was used for phonograph records, and a tape recorder was used to play many selections that had been recorded on tapes. Music was used for dancing, singing, and entertainment, and as a background during therapy sessions. Music was also played on treatment days, and at other times when the patients appeared to be unusually disturbed, for its sedative effects.

Pertinent data for evaluation of the study were taken directly from the following sources: (1) medical records, (2) ward records, (3) special incident reports, (4) entertainment listings, and (5) yard privilege records.

In addition to the information obtained from the above sources, observational records were made on the experimental patients, and ratings on the Hospital Adjustment Scale were employed before and after the introduction of the television on the control ward and before and after the closed-circuit television was introduced on the experimental ward. Psychiatric evaluations were made on a six-interval Psychiatric Scale § by the ward doctors on the experimental group on Aug. 16, 1954, on Jan. 8, 1955, and again on March 15, 1955. The first evaluations were made by the ward doctor directing the therapy from Aug. 16, 1954, until his resignation from the hospital staff, on Jan. 8, 1955. The second evaluation was made by the ward doctor directing the therapy from Jan. 8, 1955, until the end of the project, March 15, 1955.

Results

An analysis was made of the weighted scores obtained from two applications of the Hospital Adjustment Scale to determine the changes in behavior patterns for the 141 psychotic patients under study. For the 66 patients in the control group, pre- and postcommercial television, the mean score for pretelevision was 46.9 and the mean score for post-television was 52.4, or a difference of 5.5% in improved behavior patterns following the addition of television to the ward.‖ This difference was significant at the 1% level of confidence, with a standard error of the difference between means of 0.201 and a t of 2.71. A product-moment coefficient of correlation was found to be $r = +0.92$, with a standard error of r of 0.114. For the 75 patients in the experimental group, ratings of behavior pattern levels were made after 20 months of commercial television and, again, after 4 months of closed-circuit television. The mean score for postcommercial television was 48.55, and the mean score for post-closed-circuit television was 57.49, or a difference in improved behavior patterns of 8.9% following the administration of closed-circuit television. This difference was significant at the

§ Copies of this scale may be obtained from the authors.

‖ The differences in mean scores are in reality differences in percentage of the total possible score, which indicates change in rank position for a normative group, and not necessarily that the patient is 5% improved.

TABLE 2.—*Intergroup and Group Comparisons on the Hospital Adjustment Scale*

Categories	No. Patients	Mean	S.D.	S.E. Mean	r	S.E. r	t	P
Experimental Group*								
Rating 1†	75	48.55	28.11	0.326	+0.65		2.74	<0.01
Rating 2‡	75	57.49	30.18			0.116		
Control Group§								
Rating 1‖	66	46.92	32.54	0.201	+0.92		2.71	<0.01
Rating 2¶	66	52.44	30.83			0.114		
Between Groups	141	3.34	2.8	0.037	+0.86		2.4	>0.05

* The experimental group is defined as that group participating in closed-circuit television.
† Made prior to the introduction of closed-circuit television.
‡ Made following the introduction of closed-circuit television.
§ Control group is defined as that group not participating in closed-circuit television.
‖ Made prior to the introduction of commercial television.
¶ Made following the introduction of commercial television.

1% level of confidence. A product-moment coefficient of correlation was found to be $r = +0.65$, with a standard error of r of 0.116. Intergroup comparisons of these data for both the control and the experimental group are shown in Table 2.

An analysis of the data from the Hospital Adjustment Scale for the control group and the experimental group supports the hypothesis that the two samples were randomly drawn from a common population.

An analysis was made of the group data obtained from the scores of the Hospital Adjustment Scale for six areas of comparison for both the control and the experimental group (Table 3). The first comparison revealed mean group scores of 46.9 for the control group prior to any television and 52.0 for the control group following commercial television, with a total difference between mean group scores of 5.11, indicating an average of 5.1% improvement in behavior pattern levels for the control group following commercial television. The second comparison showed mean group scores of 46.9 for the control group prior to any television and 53.7 for the experimental group following commercial television, with a total difference between mean group scores of 6.76, indicating an average difference of 6.8% of improvement in behavior pattern levels for the experimental group. The third comparison revealed mean group scores of 52.0 for the control group following tele-

TABLE 3.—*Six Intergroup Comparisons of the Mean Group Scores Attained on the Hospital Adjustment Scale by the Control and Experimental Groups*

No.	Criteria for Comparison	Mean Group Score*	Mean Score Diff.†	Av. % of Group Behavior Improvement
1	Control ward prior to TV	46.92		
	versus			
	Control ward after comm. TV	52.03	5.11	+5.1
2	Control ward prior to TV	46.92		
	versus			
	Exper. ward after comm. TV	53.68	6.76	+6.8
3	Control ward after comm. TV	52.03		
	versus			
	Exper. ward after comm. TV	53.68	1.65	+1.7
4	Control ward after comm. TV	52.03		
	versus			
	Exper. ward after C-C. TV	63.11	11.08	+11.1
5	Exper. ward after comm. TV	53.68		
	versus			
	Exper. ward after C-C. TV	63.11	9.41	+9.4
6	Control ward prior to TV	46.92		
	versus			
	Exper. ward after C-C. TV	63.11	16.19	+16.2

* The Hospital Adjustment Scale is scored on a 100-point scale; each of the scores in this column is a mean group percentage of the total possible score.
† The differences in mean scores are in reality differences in percentage of the total possible score and are carried to the next column as such.

vision and 53.7 for the experimental group following commercial television, with a total difference between mean group scores of 1.65, and indicated that the experimental group had a 1.7% higher improvement in behavior pattern level at the end of 20 months of commercial television than the control group following 4 months of commercial television. Thus, at the beginning of the closed-circuit television study the behavior pattern levels for the two groups were nearly equal. The fourth comparison indicates that the control group following commercial television had a mean group score of 52.0 and the experimental group following closed-circuit television had a mean group score of 63.1, with a difference between mean group scores of 11.08, indicating an 11.1% average group improvement in behavior pattern levels for the experimental group. On the fifth comparison the mean group scores were 53.7 for the experimental group following commercial television and 63.1 for the same group following closed-circuit television. The difference between mean group scores was 9.41, indicating a 9.4% average group improvement in behavior pattern levels within the group following the administration of closed-circuit television therapy. The sixth comparison was made between the experimental group following closed-circuit television therapy and the control group prior to any television. This comparison revealed mean group scores of 63.1 and 46.9, respectively, with a difference of 16.19, indicating a 16.2% average group improvement in behavior pattern levels following closed-circuit television therapy as compared with that for the group with no television.

The analysis of the subscores of the Hospital Adjustment Scale covered the areas of (1) communication and interpersonal relations; (2) work, activities, and recreation, and (3) self-care and social responsibility. The range of improvement under the first category for the experimental group was from +1 to +80, whereas under the same category the range of improvement for the control group was from +1 to +37. In the second category the range of improvement for the experimental group was from +1 to +90, whereas the control group range was from +1 to +44. In the third category the range of improved behavior for the experimental group was from +1 to +94, and for the control group the range was from +1 to +53.

The Psychiatric Evaluation Scale was a device, especially designed for use in this study, which rated patients on a six-interval scale. The results of the evaluations made on this scale by the ward doctor are shown in Table 4. The following results were obtained for the 75 patients in the experimental group who were receiving closed-circuit television therapy: Evaluation of 4 of the patients indicated that their conditions had become worse; 8 patients showed no improvement; 12 of the patients were

TABLE 4.—*Comparison of Psychiatric Evaluation Scores for Seventy-Five Subjects Under Study*

Category of Improvement*	Rate of Improvement	No. Patients	Patients Percentage
Worse Deteriorating	0	4	5.33
No change	0	8	10.67
Borderline toward slight improvement	0.5	12	16.00
Slightly improved	1	18	24.00
Improved	2	19	25.33
Much improved	3 & 4	11†	14.67
Markedly improved	5 & 6	3‡	4.00

* Slight improvement in one area, 1. Slight improvement in two areas or markedly improved in one, 2. Marked improvement in one area; slight in one, or slight in three, 3. Marked improvement in two areas; marked in one, and slight in two, 4. Marked improvement in two areas; slight in third, 5. Marked improvement in all areas, 6.

† Eight patients rated 3; three patients rated 4.

‡ Two patients rated 5; one patient rated 6.

rated as borderline with a possible slight tendency toward improvement; 18 patients clearly showed improvement in one area and were rated as slightly improved; 19 patients were rated as improved; 8 patients were rated as much improved, and 2 patients were rated as markedly improved.

Results relative to each of the hypotheses are now presented. Hypothesis 1 was tested by six comparisons, as shown by Table 3. A further test of the hypothesis was made by an analysis of the different types of therapy used in this study. It was also tested by intergroup comparisons for the control group.

Forty-two patients within the experimental group received no other therapy than that presented over closed-circuit television, and this group responded with a 12.4% average improvement in behavior pattern levels, as measured by the Hospital Adjustment Scale. A further evaluation was made on the Psychiatric Evaluation Scale, which indicated an average patient improvement of 11.43%. The statistical data convincingly supports Hypothesis 1. Therefore it is concluded that therapy can be administered effectively in a simulated face-to-face situation through the medium of closed-circuit television, giving the impression of individual therapy, while administering to a mass audience.

Hypothesis 2 is supported by the high percentage of improvement shown by those patients receiving no therapy other than closed-circuit television.

By means of closed-circuit television, motion pictures dealing with mental hygiene and other educational subjects, filmstrips, and other suitable materials can be presented as often as desirable to reinforce, by repetition and consistency, the basic principles underlying good mental health. Orientation programs, interpretations of hospital and ward routines, and programs of general education and instruction can also be presented effectively to a mass audience through this medium.

Further support for Hypothesis 2 may be found in the data obtained from the intergroup comparisons of the Hospital Adjustment Scale (Table 2). In the area of work, activities, and recreation, the scores reveal a 69.3% mean difference in improved behavior patterns for the experimental group following closed-circuit television therapy. The range of improvement in this area was from +1 to +90. The unimproved behavior range for this area was from −1 to −34, with 6.67% of the patients making no change. Data obtained from the Hospital Adjustment Scale further revealed that 64% of the improved behavior shown within the experimental group was in the area of communications and interpersonal relations, with a range of improvement of from +1 to +80.

An analysis of the population status of the experimental and control wards was made at the termination of the program. During the period the two wards were evaluated the population changes shown in Table 5 occurred.

TABLE 5.—*Population Changes During Program of Study*

Change	Experimental Ward	Control Ward
Discharges	2	0
Transferred to open wards	3	0
Granted indefinite leave	4	1
Granted yard privileges	18	4
Granted longer definite leaves	11	2
Total population changes effected	38	7

The control-ward changes took place during the four months following the addition of commercial television, and the experimental-ward changes took place during the four months that the closed-circuit television therapy program was presented.

On March 10, 1955, the closed-circuit television program was demonstrated before 11 different departments of the hospital. Each observer was requested to evaluate the potential usefulness of this medium in relation to his individual field of interest. A total of 49 persons evaluated the program as a medium for use in mental hospitals. The responses derived from the six-point questionnaires presented to each of the hospital personnel are as follows:

1. "Do you feel that closed-circuit television is of value in your field?" One hundred per cent answered, "Yes."

2. "What are some possible uses for closed-circuit television in your work?"¶ The types of responses received and their percentage of occurrence are shown in Table 6.

TABLE 6.—*Uses of Closed-Circuit Television*

Response	Percentage
Staff training	10.0
Work placement	2.5
Family care	2.5
Group therapy	37.5
Orientation programs	10.0
Education and training	72.5
Interviewing techniques	15.0
Individual therapy	12.5
Entertainment	7.5
Staff clinics	15.0
Demonstrations	15.0
Observation of patients	30.0
Psychotherapy	7.5

3. "Do you feel that closed-circuit television can be of value in extending technical training facilities provided at this hospital?" One hundred per cent answered, "Yes."

4. "What limitations in the value of closed-circuit television do you recognize or see from the demonstration?" The responses are shown in Table 7.

TABLE 7.—*Limitations in Value of Closed-Circuit Television*

Response	Percentage
Will not replace individual relations	20.0
Might involve additional workers	2.5
Need to use carefully	2.5
No limitations	62.5
Could foster unrealistic thinking	2.5
Too expensive	7.5

5. I believe closed-circuit television for hospital use is represented by the following categories: Very limited, 0; limited, 10.0%; limited to specific subjects only, 17.5%; many users, 52.5%; and almost unlimited, 20.0%.

6. "Please list your specific suggestions for using closed-circuit television in your field of interest." Responses are listed in Table 8.

TABLE 8.—*Suggested Uses of Closed-Circuit Television in Medicine*

Suggestions	Percentage
Inservice training	5.0
Patient contact	12.5
Relative education	2.5
Orientation	2.5
Education	35.0
No comment (no suggestions)	52.5
Group therapy	5.0
Psychotherapy	7.5
Staff conferences	2.5
Entertainment	2.5
Patient observation	17.5
Saving on time and money	2.5
Expedite supervision	2.5

Comment

The two hypotheses stated at the beginning of this study were supported by the data obtained. A significant change toward better hospital adjustment and improved behavior patterns and activity levels was shown by these data.

The important variable of extra attention, given to the isolated patients, threatened to contaminate the results of this study. In an effort to control this variable, the following procedure was followed: From Aug. 1, 1953, to March 15, 1954, the research team worked exclusively with the control group. It was during this period that the rating/rerating scores were obtained on the Hospital Adjustment Scale, as well as the installation of a commercial television set on the ward. The period of extra attention to this group covered the same amount of time as the period of extra attention given at a later date to the experimental group. From Aug. 1, 1954, to March 15, 1955, the control group was rigidly ignored by the research team, and all attention was concentrated on the experimental group. In this manner the variable of extra attention was equated.

For the control group, the independent variable was the addition of a commercial television set on the ward, and the dependent variable was the rating/rerating on the Hospital Adjustment Scale. For the experimental group the independent variable was the use of therapy via closed-circuit

¶ Questions 2 and 6 were not restricted to any specific number of statements. A total of 209 statements were obtained. For more concise reporting, these statements were classified under the general headings given.

television, and the dependent variable was the rating/rerating on the Hospital Adjustment Scale.

A Pearson product-moment coefficient of correlation revealed an r of +0.92 between the two separate ratings of the control patients. The high value of r indicates that there was very little shift in relative positions within the group, in post-television as compared with pretelevision. An examination of the individual shifts in position shows that the greatest changes were made by the patients' ranking (if measured by quartiles) in the second and third quartiles, while those in the extreme positions (first and fourth quartiles) shifted very little.

For the experimental group a correlation of +0.65 was obtained from a comparison of the two separate ratings. This moderate correlation would indicate some rather extreme shifts in position within the group. An examination of the individual shifts indicates that the greatest changes were made by the patients ranking in the first and second quartiles, while the patients in the third and fourth quartiles made relatively little shift in position.

Thus it can be seen that the patients in the experimental group receiving closed-circuit television therapy made the most drastic shifts in improvement, with the patients rating the lowest prior to closed-circuit television improving rapidly, in contrast with those patients originally considered less seriously ill.

An analysis of the data as reported on the Hospital Adjustment Scale revealed certain differences of response to the program by the differing diagnostic categories of patients represented in the study.

One of the subgroups showing a high degree of average improvement was the group classified as catatonic. In this category of illness, 10 of the 13 patients (77%) showed an average of 23% improved behavior changes. These patients had been hospitalized for an average of six years longer and were on the average 11½ years older than the three patients showing no improvement.

Within the subgroup category of schizophrenia, undifferentiated, other types mixed, 9 of the 15 patients (60%) were classified as showing an average of 28% improved behavior patterns. These nine patients were 4 years older on the average and had been hospitalized for one year less than the six patients showing no improvement.

Among the patients classified under involutional psychosis, four out of six (67%) showed an average of 33% improved behavior patterns. In this group, those patients rated as improved had been hospitalized for an average of four years longer than the two patients rated as unimproved. The average ages for the two groups were the same.

There were 13 patients classified under the category of hebephrenia. Of this group, eight patients (62%) were rated as having 24% improved behavior patterns. This group, on the average, was one year younger and had been hospitalized two years longer than the five patients showing no improvement.

Of the four patients classified under manic-depressive, one (25%) showed a 3% improvement in behavior patterns. This patient was one year younger but had been hospitalized for five years longer than the average of the three patients in the unimproved group.

Within the diagnosis of psychosis with mental deficiency there were four patients, only one of whom (25%) showed any improvement, and this amounted to only a 5% improvement in behavior patterns. This patient was 10 years younger but had been hospitalized for 16 years longer than the average for the three patients showing no improvement.

Only one patient was classified as manic-depressive with neurosyphilis. This patient had a 45% improvement in behavior patterns. The one patient with the diagnosis of psychosis with arteriosclerosis showed a 29% improvement in her behavior patterns. There was no improvement noted in the behavior patterns for the one patient diagnosed as having Korsakoff's psychosis or for

the patient diagnosed as psychosis associated with organic brain disease.

Forty-two patients from the experimental group received no somatic treatment and no therapy other than the motion pictures and programs televised by closed-circuit television to the experimental group. Of these patients, 19 made improved changes in behavior patterns; 19 made slight negative changes in behavior patterns, and 4 patients remained static (no change), as measured by the Hospital Adjustment Scale. When rated on the Psychiatric Evaluation Scale, 35 of these patients made improvement in one or more areas, from slight to marked, with a range of from 0.5 to 4; 5 patients made no change, and 2 of the patients were considered worse when rated by the psychiatrist.

The diagnostic classifications for the group receiving only television therapy, and their behavior change, as measured by the Hospital Adjustment scale, are shown in Table 9.

During the study two types of therapy were used continuously: (1) panel and group therapy sessions and (2) selected motion pictures. In an effort to test as many techniques as possible in the length of time allotted for the study, other therapies were employed for short periods: music therapy, art therapy, psychodrama, individual therapy, and question-and-answer programs, all of which were televised to the experimental group by closed-circuit television.

The plan to use motion pictures for therapy was based on observations made in the two previous studies, wherein patients identified with the performers in films presented on the commercial television programs. In view of certain attitudes revealed by the patients in the two previous studies, a major problem was to attain the understanding and cooperation of the patients with a short-term therapeutic program. Some of the patients' attitudes resulted from the following factors:

1. They were chronically ill psychotic patients.

2. Many of these patients had not understood or cooperated with previous programs of treatment earlier in their hospitalization.

3. They were isolated in closed wards with very little outside contact.

4. After years of hospitalization, many of the patients had given up all efforts to recover and apathetically accepted their condition as hopeless.

5. Many of these patients had developed the attitude that no one cared about them. Hospital overcrowding and understaffing contributed greatly to this feeling, since the doctors and psychiatric technicians were too

TABLE 9.—*Diagnostic Classification and Behavior Changes in Group with Television Therapy Only*

Diagnoses	Patients Improved	Av. % Improvement	Patients Unimproved
Schizophrenia			
Hebephrenic	6	18	4
Catatonic	5	15	2
Undifferentiated: mixed	6	22	3
Paranoid	0		5
Total	17	18	14
Psychoses			
Involutional psychosis	1	15	1
Manic-depressive, depressive	0		1
Mental defective with psychosis	0		1
Total	1	15	3
Organic psychoses			
Psychosis with arteriosclerosis	1	29	0
Psychosis associated with organic changes of nervous system	0		1
Korsakoff's psychosis	0		1
Total	1	29	2
Complete total	19	18.3	19

busy with the care of all of the patients to devote much time to each individual. The mere fact that they were hospitalized was considered by many of the patients as complete and total rejection.

6. Many of the patients were hostile, suspicious, and fearful of attention, preferring to remain unnoticed in the group, since individual attention often resulted in some unpleasant experience.

Since the attitudes enumerated above were an essential factor in planning the total therapeutic program, it was necessary to consider what educational techniques would best influence these particular attitudes. An attempt was made to determine the effectiveness of televising certain audiovisual educational aids in an effort to bring about the desired results through a program of therapeutic reeducation.

The research team selected motion pictures and planned therapeutic programs that they felt would best meet the major challenges common to mental illness. How to effect motivation within the patients to want to adjust to life outside the hospital, and to offer sufficient incentives to make it worth while for them to expend the effort necessary for recovery were two of the major problems encountered.

The film programs were developed on a graduated scale, beginning with general-interest subjects and progressing to mental hygiene films dealing with emotional problems. From the beginning of the study the response to the films was excellent. Films receiving the most enthusiastic response were those from the "Marriage for Moderns," the "Adolescence," and the "Mental Mechanism" series.

Responses were expressed in several ways. After the showing of the series on grooming and posture, the patients responded by wearing clean, and when possible new, dresses, getting permanent waves, manicuring their nails, and taking an active interest in personal hygiene. After the films on dressmaking, and the fashion industry, some of the patients planned to make dresses and model them for the group.

Samples of the verbal responses made by the patients to certain films are listed below. These statements, copies verbatim, are as follows:

1. Following the picture on "Social Development"[6]: "They act just like my children did. This certainly takes us out of ourselves and makes us think of going home."

2. Following the film, "Overdependency"[6]: "These films certainly have a lesson to them. They are wonderful. Films for entertainment are all right, but it's the first time anyone ever thought we had enough sense to understand or learn anything. Please keep showing them."

3. After the film, "Improve Your Personality"[7]: "These movies are wonderful . . . they make our discouragement less, and make us more broadminded . . . They give us some outlook and hope for the future."

In an effort to obtain a random sampling of patients' attitudes in regard to the overall program, 10 patients were asked the following questions: 1. Do you like the movies you have seen? 2. Which movies did you like best? 3. Do you like the group discussions over TV? 4. What have you learned from the TV discussions? 5. Have you any suggestions to make concerning the programs?

Responses to the above questions can be summarized in this manner: 1. They definitely like the movies, especially the mental hygiene films. The comedy films were entertaining, but the mental hygiene films, they stated, "make us more broadminded and bring out our evil thoughts." "They make our discouragement less." 2. The patients who had participated in the group discussions remarked, "It helps us to work through our problems by discussing them." Those who had not participated in the discussions remarked, "Listening to the group discussions takes a person away from their troubles and gives them a different outlook on life." "I suddenly realized that I wasn't the only one with problems, and you know something funny, when they started talking about ways to solve their problems I found myself trying to solve mine." All of the patients interviewed expressed strong desires for more group discussions, and more movies, especially on mental hygiene.

Music therapy was an integral part of the programing and served in several ways. All group therapy sessions and films were preceded and followed by a 10-minute program of music. Art therapy sessions, usually conducted without comment, were accompanied with music, and often, when no television program was being broadcast, music alone was played through the audio connection to the ward. All in all, it is safe to say that music was utilized whenever possible in the program for its varying effects. It was found that certain types of music brought about certain generalized responses. It appeared to the researchers that initial contacts established with some of the more withdrawn patients were accomplished during or after some type of music therapy; for example, several chronic catatonic patients who would not respond to any other stimulus would respond to certain tunes when they were played, while apparently ignoring others. Inasmuch as nearly all of the patients responding to music indicated certain preferences, future studies should include a fairly wide repertoire, in order to satisfy as many requests as possible.

All age groups participated in the art therapy program, apparently without feeling the pressure of competition, and developed some status within the group for work that was admired and pointed to as an example of success. This type of therapy was well received and appeared to stimulate the patients into making positive behavioral changes by their own unguided efforts. By having the art supplies readily available on the ward, and seeing motion pictures and other programs dealing with art, the patients were encouraged to greater participation in the activity. In order to paint or draw, it was necessary for a patient to share, with others, a table in the day hall. This arrangement forced the patients to sit in groups, resulting in socialization, which helped them to develop better techniques for further social adjustment.

The results of this study indicated that therapy presented over closed-circuit television was partially responsible for the behavior changes of each of the improved patients in the experimental group. Further, this therapy was the major factor in bringing about the improved behavior changes, as rated by the Psychiatric Evaluation Scale, for 35 patients receiving no somatic treatment or therapy other than by closed-circuit television. Offering therapy by this medium becomes more practicable and appears to be more meaningful when patients actively participate as the therapeutic agents in the programing.

Summary

This study has attempted to investigate the effects of therapy administered by closed-circuit television in relation to the behavior pattern changes, interpersonal relationships, and hospital adjustment of psychotic patients.

One hundred forty-one chronically ill psychotic female patients, hospitalized at Agnews State Hospital, Agnew, Calif., were the subjects for this investigation. They were classified into two groups: the control group, composed of 66 patients, and the experimental group, composed of 75 patients.

A comparison was made of the performance of each group under two conditions. The control group was rated pre- and post-commercial television, and the experimental group was rated after commercial television and after closed-circuit television. The data were treated statistically by (*a*) comparisons made of the ratings of each group on the total score and three subscores of the Hospital Adjustment Scale; (*b*) computation of the difference in percentage values of changed behavior, according to diagnoses, for the experimental group; (*c*) comparison of the evaluations made by the ward doctor on a six-interval scale, giving medical estimates of the degree of change occurring for each patient; (*d*) computation of the percentage values resulting from intragroup behavior changes as related to the therapies employed.

Hypothesis 1, that therapy can be administered effectively in a simulated face-to-face

situation through the medium of closed-circuit television, giving the impression of individual therapy, while administering to a mass audience, was confirmed.

Comparisons were made for the control group (no television and commercial television), and the experimental group (commercial television and closed-circuit television); the results of these comparisons were based on scores computed from the rating/rerating for each group on the Hospital Adjustment Scale (Table 3). These data revealed that the addition of a commercial television set on the control ward improved group behavior patterns 5.1% in three months, and the addition of closed-circuit television to the experimental ward, following 20 months of commercial television, improved group behavior patterns 9.4%. The use of closed-circuit television plus commercial television resulted in an average improvement in behavior for the experimental group of 16.2%. Further group comparisons indicated that Hypothesis 1 was supported.

From these findings, it is concluded that mentally ill patients will improve significantly in behavior patterns when given therapy by closed-circuit television in the areas of communication and interpersonal relationships, socialization and self-care, and work, activities, and recreation, as measured by Ferguson, McReynolds, and Ballachy's Hospital Adjustment Scale.[1] It is further concluded that psychotic patients will improve (*a*) by the amelioration of symptoms of mental illness, (*b*) in relationships (social and interpersonal), and (*c*) by response to stimuli, as evaluated by the ward doctor on the Psychiatric Evaluation Scale.

Support of Hypothesis 2 was found in the range of improvement reported for the experimental group as contrasted with that for the control group in the areas of communication and interpersonal relations. Further support was found for that part of Hypothesis 2 which stated that programs of general education and instruction can also be presented effectively to a mass audience through this medium.

It would appear that, in order to cope with the increasingly difficult situation of overcrowding and understaffing faced by most of mental hospitals, some new methods of administering therapy must be instituted. Though many techniques of therapy have been developed, they are valueless unless they reach the patient personally. Many worth-while therapies are invalidated because of the inability to deliver them economically to a large number of patients. It would now seem, as a result of the findings of the present investigation, that perhaps these worth-while therapies can be used much more extensively than in the past through the medium of closed-circuit television. Certainly, the results of the present investigation should warrant further exploration of this area.

Agnews State Hospital.

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Lead Poisoning in Children

A Study of Forty-Six Cases

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Forty-six children having confirmed cases of lead poisoning were hospitalized in Chicago in 1953 and 1954. This article summarizes the epidemiological and psychological findings for both years and reports on a follow-up psychological study of the first group two years after their acute illness.

The same investigative procedures and psychological techniques were used in 1953 and 1954. A comprehensive report on the cases discovered in 1953 and a description of our procedures has already been published.[1] The clinical, laboratory, epidemiological, case history, mental, and emotional findings were very similar for the two years. Our present, larger, sample and consistent findings allow us to make more precise statements about this public health problem.

Epidemiology

The epidemiological data show children between 1 and 4 years of age to comprise about 90% of the cases. The same proportion reside in the poorest slum areas of the city, a few being in lower-middle-class neighborhoods. The homes were for the most part dilapidated, submarginal apartments. This accounts for the presence of old, peeling paint, the lead-containing substance most commonly ingested. The families from which the patients came averaged four children. In some cases the parental supervision seemed good, in others poor. The patient group seemed no different in this respect from the average household in the rest of this lowest socioeconomic class.

It is curious to note that of these 46 cases, 43 were first hospitalized during the five months May through September. Twenty-five were admitted to hospitals in August. Although these children ingest small quantities of lead all year, a serious crisis occurs during warm weather. Fatalities were spread evenly through the five-month warm season. In the second year of the study an attempt was made to determine the role of exposure to sunlight and oral administration of vitamin D relative to exacerbation of this illness. It was difficult to get clear, reliable data on these questions, but there seemed to be no significant trend for the group.

Summary of Case Histories

Of the two-year total of 46 cases discussed here, 13 were fatal and 1 patient moved out of the state shortly after release from the hospital. All of the remaining 32 children were given psychological examinations. This psychological study included (1) a detailed developmental history, (2) the Vineland Social Maturity Scale, (3) the Kuhlmann Tests of Mental Development, and (4) observations of spontaneous and elicited behavior during play and examination sessions. These methods have been fully described previously.

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This study was initiated and carried to completion under the auspices of Dr. Herman N. Bundesen, president of the Chicago Board of Health. Mrs. Carol K. Watkins, psychiatric social worker of the Chicago Board of Health, collected the developmental histories, which contribute significantly to the completeness of the report. Dr. Irene C. Sherman, Chief of the Mental Hygiene Section, Chicago Board of Health, participated in the planning, progress, and reporting of this project. The better features of the psychological study are attributable to her supervision and advice.

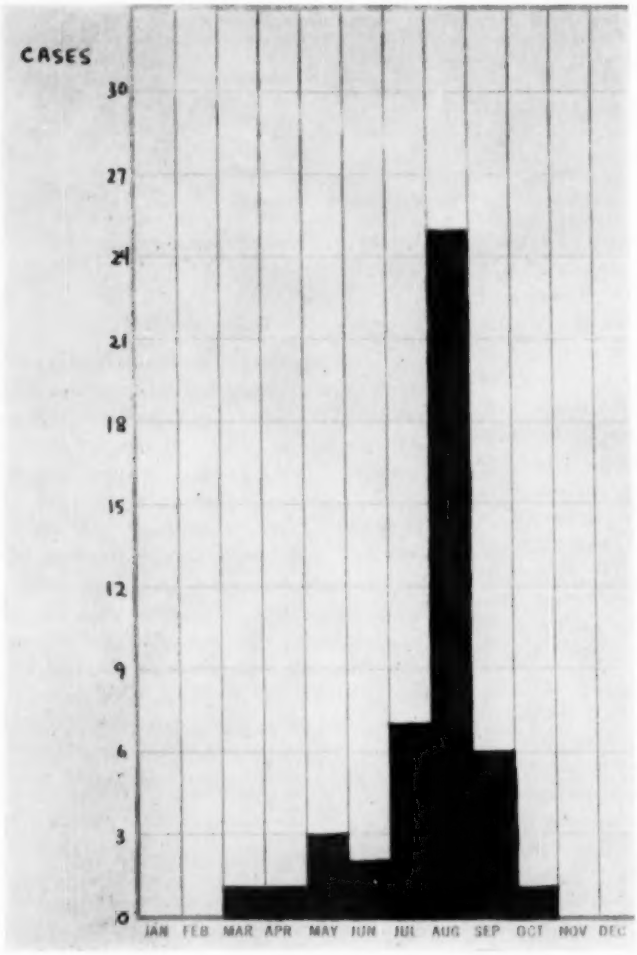

Fig. 1.—Hospital admissions of children with lead poisoning in 1953 and 1954, by months.

In general, the 32 children studied were not retarded in development prior to illness. It had been thought by some that only retarded children engage in pica and thus become poisoned, by reason of inability to discriminate between edible and nonedible substances. Our data cannot support this hypothesis.

Specific questioning relating to motor development (manipulation and locomotion), language development, and emotional stability (including response to others and reaction to minor frustration) indicates that most of the patients were developing normally in the motor and mental areas prior to illness, but about half were showing emotional behavior which the mothers considered "not as good as" that of patient's siblings when at the same age. Whether this is a sign of a basic ego weakness or of particular environmental pressures we have no knowledge.

Medical histories revealed only 8 of the 32 children to have been ill, except for colds and slight fevers, at any time prior to lead poisoning.

Pica and Eating Habits

The universality of pica is a finding again to be underlined. Pica was found in 31

TABLE 1.—*Rate of Development Before Lead Poisoning*

Kind of Development	Slightly Advanced	Normal	Retarded	Doubtful or No Data	Total
Motor	5	21	3	3	32
Language	2	17	6	6	31*
Emotional	5	13	14	2	32

* One child ill with lead poisoning at 8 months of age—before language normally appears.

of 32 cases and probably occurred in the one case without the parents' awareness. About three-fourths of the children showed a general pica, in which numerous nonfood substances were eaten. In the remaining fourth only one or two specific substances were consumed. This abnormal eating is a motivated behavior not cured by distracting the child with other activities. Where used, alternative chewing objects did not curtail this dangerous activity. Sometimes not even spanking kept the child from nibbling at the sites of peeling paint. The parents of a girl who loved to eat cigarette ashes placed candy on the table near the ash tray. She ignored the candy and scooped up the ashes.

Children addicted to pica thus discriminate their favorite substances from food and know they are not supposed to eat the nonfood substance. The latter awareness is shown by their furtive eating of this substance. Most of the nonfood substances so consumed are dry plaster, dried paint, ashes, dust, and cloth. Yet these children's food preferences do not in general follow this textural pattern. Although food habits, weaning, and early feeding procedures were inquired about, no oral training patterns or dietary deviations emerged which were at variance with normal.

It is felt that pica is an emotionally caused behavior, perhaps related to feelings of aggression. As to the way in which the children engaged in their pica and the way in which they mouthed toys and other objects, it is significant to note that 21 bit, 3 both bit and sucked, 3 only sucked, and 1 reportedly did neither. Data on the remaining four cases were uncertain. Six repeatedly bit playmates and siblings; two of these tried to bite their mothers. Research into the mother-child relationship in cases of pica might be rewarding.

Acute Phase

The acute phase of childhood lead poisoning and the emergency hospitalization in over half the surviving cases were ushered in by a week or 10 days of signs of cerebral irritation. These included fatigue and one or more of the following symptoms: extreme irritability, fearfulness, withdrawal, weakness, and crying for no apparent reason. In only four cases was this syndrome completely absent. Vomiting and constipation were also common. The severe stage was marked by convulsions, coma, and, in a few cases, partial paralyses. The severe illness caused gross regression in the children. During hospitalization most patients lost bowel and bladder control and some or all of their speech.

Psychological Study

Psychological examination six to eight months after discharge from the hospital revealed the group to be markedly retarded and to show signs of brain damage. The average chronological age at time of examination was 3 years 2 months. The average mental age was 2 years 4 months, with an average I. Q. of 74. The accompanying graph (Fig. 2) shows the frequency distribution of the scores of our patients as compared with the distribution of scores of the normal child population actually used by Kuhlmann in standardizing the test.[2] The drastic downward displacement of scores of the lead poisoning group is to be noted.

Considering the cases individually, it is noted that 27 of the 32 children were seriously retarded at time of testing, whereas

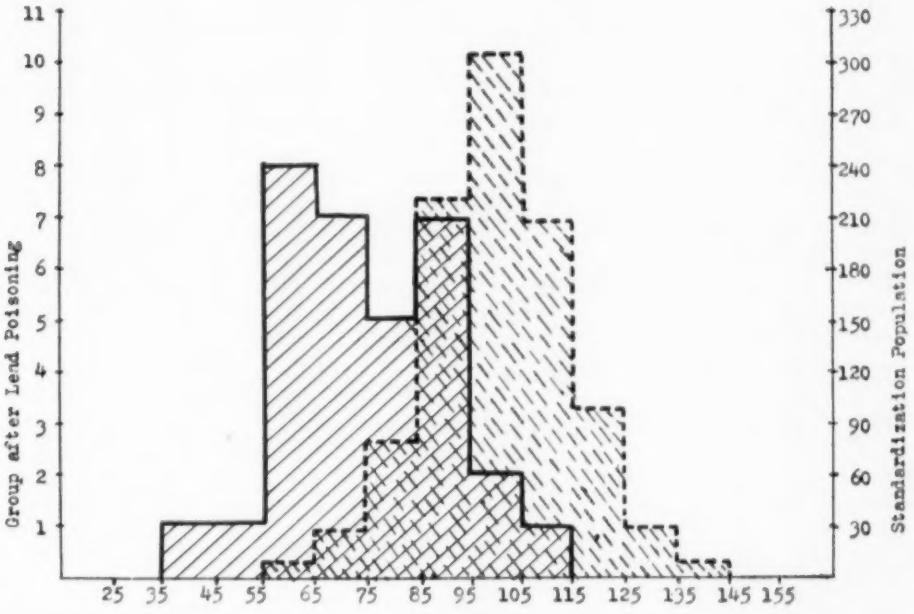

Fig. 2: Distribution of Intelligence Quotients (Equated for sample size)

Group after Lead Poisoning. Ages 2 years to 5 years. N= 32

Kuhlmann's Standardization Group. Ages 6 months to 6 years. N=973

before lead poisoning only 7 seemed to have had retardation of general development. Impairment of speech, ranging from marked difficulties in articulation to severe reduction of verbalization, is a frequent sequela of this malady, five children having lost speech entirely. Even six months later at examination their communication was largely by cries, gestures, and unintelligible efforts at phonation. In all, 18 children suffered speech impairment from severe lead poisoning; some of these, however, recovered rapidly. Ten children (including some of those noted above) suffered damaged coordination of small muscles. Drooling and difficulty in grasping and in directing movements of the arms were observed. About one-fourth of the cases showed neither of these specific difficulties.

Study of the successes and failures on the tests (scatter analysis) shows that these patients have greatest difficulty in tasks calling for naming of objects, visual memory, and simple conceptualizing. Copying a circle was especially difficult. In eight cases this was the first failure on a scale of tasks of gradually increasing difficulty. Eleven children could only scribble jerkily when presented with paper and pencil. Although visual memory was poor, these children did comparatively well on auditory memory. Repeating digits and sentences after hearing them was the highest test passed by some patients. The patients responded copiously to pictures, but qualitatively their responses were a barren enumeration of parts of the picture. The genetically more advanced levels of description and interpretation were notably absent.

After recovery from the acute phase of poisoning, emotional instability, as evidenced by temper tantrums, frequent whimpering, fighting, or excessive fearful withdrawal, was either reported by mothers or observed

by the examiner or both in 24 children. Seventeen of these children were reportedly more unstable now than before their illness. Thus, we see that, although emotionally immature children were present in the group prior to the illness, the supervention of lead poisoning further impeded the emotional maturation both of those children previously stable and of those previously unstable. Difficulties in relating to siblings and playmates were prominent.

Social maturity as measured by the Vineland Scale was below average, yet significantly higher than the intelligence quotient. Twenty-one children scored social quotients below average (100), while 11 scored above average. Such things as independence, self-help in eating and cleanliness, and level of play are measured by the Vineland Scale.

Following lead poisoning these children were extremely distractible. Neither during play nor testing could they maintain attention for any period of time. They were not distracted by extraneous sights and sounds in the room (of which there were few), but, rather, by internal factors. Their eyes wandered; some seemed at times "in another world." Some had difficulty remaining seated even for a few minutes at a time and wandered about in a manner typical of motor-driven, organic brain-damaged children, which indeed they are. Using a five-point scale of distractibility patterned after that in the 1937 Stanford-Binet Intelligence Scale, the pattern shown in Table 2 emerged.

TABLE 2.—*Distractibility Scale*

		No. of Cases
Minimal	Completely absorbed by task	0
Low	Little interference from distracting stimuli	1
Average	Outside stimuli do not impair efficiency	3
Great	Child easily distracted by extraneous stimuli or by own ideas but returns readily to task	16
Extreme	Abstracted; difficult to get and hold attention	12

With reference to the possibility of recurrence of severe lead poisoning, the child's present eating behavior was inquired about. It was a source of great concern to learn that in some children the habit of pica continued. Habitual pica was present in 10 cases at time of examination. In nine others a few isolated instances of pica had occurred. The remaining 13 children had completely stopped such behavior. In 1954 a series of questions on present eating habits and food likes and dislikes was asked. The tabulation of these data was examined by an experienced nutritionist,* who concluded that these eating patterns did not differ consistently from those of normal children of this age. No dietary factors seemed to relate to the presence of pica in those children in whom it continued.

Follow-Up Study

The group of children surviving lead poisoning in 1953 were examined early in 1954, as reported previously, and the findings presented in Table 2. They were individually reexamined in the summer of 1955. This follow-up (retest) was conducted 20 to 24 months after hospitalization for severe lead poisoning and 13 to 17 months after the first testing. Of the 16 survivors of the severe illness, 15 were tested in 1954; 14 of these 15 were retested in 1955.

Seven of the fourteen children retested showed normal growth in mental ability during the year and also seemed to have made up part of the loss incurred during severe poisoning. This is shown by gains in mental age and in intelligence quotient. In only three of these cases, however, was this gain in intelligence quotient statistically significant. Five others maintained a steady intelligence quotient, indicating that the child progressed, but at an impeded rate of maturation and learning. The remaining two children suffered a loss in intelligence quotient, gaining only 2½ and 5½ months, respectively, of mental age in the 14 and

* Mrs. Pearl S. Camstra, Chief, Nutrition Section, Chicago Board of Health.

16 months between their first and second test. Clearly these two children are severely damaged and prognosis is extremely poor. The total group averaged a gain of 6 I. Q. points between test and retest. This gain is not significant statistically.

On the positive side, three children improved their performance by 16, 21, and 28 points in intelligence quotient, respectively. This gain was largely accounted for by recovery of speech and increased and better-integrated drive. Whereas at first test these three children were impaired in speech, listless, and incapable of sustained effort—even little negativistic effort—at retest they communicated readily and showed more energy and seeming purpose in their responses to the surroundings. The improvement in these cases was consistently associated neither with reduced distractibility nor with less "scatter of score."

The parents' subjective appraisal of the children indicated greater improvement than did test results. Such reports as "speaks more plainly now," "has regained bladder control," "now helps younger brother" are not reflected in test scores. It must be remembered, of course, that mothers of children who have suffered setbacks have need to maximize even small improvements made by their children.

The test behaviors, observations of play, and parents' reports were combined to give a total behavioral picture for each child. When the report on each child was analyzed according to motor, language, and emotional control aspects, the following trends from before illness to present status emerged and are shown in Tables 3, 4, and 5.

Tables 3 to 5 show a common picture of these children's histories—an average development in early childhood, a severe setback between the ages 1 and 4 years, caused by lead poisoning, and a gradual, but incomplete, trend toward recovery by one-fourth to one-half the group.

Two years following hospitalization, the damaging effects of lead can still be seen, especially in impaired speech (seven cases had impediments of articulation at retest) and disturbed emotional control (nine cases). Fine-muscle coordination, impaired in a few cases at first examination, improved

TABLE 3.—*Motor Development*

Time \ Rating	Very Poor	Below Average	Average	Above Average	Inadequate Data	Total
Before illness (from history)	1	—	11	3	—	15
Convalescence						
8 mo.	2	8	5	—	—	15
23 mo.	1	2	9	2	—	14

TABLE 4.—*Language Development*

Time \ Rating	Very Poor	Below Average	Average	Above Average	Inadequate Data	Total
Before illness (from history)	1	1	10	—	3	15
Convalescence						
8 mo.	6	6	3	—	—	15
23 mo.	3	4	6	1	—	14

TABLE 5.—*Emotional Stability*

Time \ Rating	Very Poor	Below Average	Average	Above Average	Inadequate Data	Total
Before illness (from history)	—	5	9	—	1	15
Convalescence						
8 mo.	6	7	1	1	—	15
23 mo.	3	6	5	—	—	14

to a greater degree at retest than did speech and emotional control.

Relation of Treatment to Outcome

In comparing the original clinical picture of each child during severe illness with the outcome of the case, it was found that no one or two clinical signs or symptoms, as recorded in the hospital medical charts, were prognostic of the final outcome. Encephalopathy was noted in almost all the cases. The fatalities, the worst defectives, and the survivors with better recovery did not differ *as groups* on the basis of clinical symptoms or laboratory findings. Specifically, there was no correlation between blood lead level or low hemoglobin and the outcome of the case. Although a large share of the children who had convulsions died in the hospital, the survivors were equivalent with respect to mental tests to the survivors who had no convulsions.

Treatment of the acute phase of lead poisoning consisted of supportive or symptomatic therapy with or without use of edathamil calcium.† In no case was dimercaprol (BAL) used. Comparing kind of treatment and its timing with mental level two years later, no clear group-wide superiority was seen in children given edathamil calcium before encephalopathy, those given edathamil calcium after encephalopathy, or the group treated symptomatically. Our information as to the clinical picture and severity of condition during hospitalization is based only on abstracts of the medical records and is thus definitely incomplete. It cannot be assumed that the groups treated before and after encephalopathy were equivalent in other critical factors, and thus no estimate of the efficacy of treatment should be made. The small size of the subgroups contributes statistical unreliability, further precluding inference along these lines.

Specific Retest Factors

In addition to the general findings sketched above, certain specific test data are of interest. Analysis of the best successes and lowest level of failures (scatter analysis) shows two patterns emerging in the group. The four children with lowest general ability made their earliest failures because of impairment of speech function. They were either so limited in expression that they could not make simple descriptive or enumerative responses or had such trouble in articulating words that they could not repeat words of the examiner or make their own spontaneous expressions understandable. In a few cases even the mother could not understand some of her child's utterances.

The children with generally better performance had no such defect in the verbal area, some making their highest scores on vocabulary and the giving of information, although at times with difficulty in articulation. In these children the outstanding disability was one of attention and memory. Some items were missed because the children could not maintain attention to the directions. Other tasks were begun but not completed because, even with the support of the examiner, attention could not be sustained.

Memory items account for the earliest failures in 5 of the 10 children scoring highest in general ability. The pattern of highest items passed was more heterogeneous, with tracing and information about simple objects most successfully handled.

Measure of variability or irregularity of performance (scatter) is standardized on the Kuhlmann Tests. Both test and retest show a slight tendency toward greater than average scatter, but one not statistically significant.

At original testing most children were unable to use a pencil and paper. Drawing behavior was in general much improved over the original testing to the extent that the Goodenough Draw-a-Man test could be administered in 10 cases.[3] This is graded on the child's differentiation of body parts, awareness, and inclusion of detail, and on proportion, but it does not credit artistic

† Calcium ethylenediaminetetraacetic acid; also called Versene.

skill. It is also thought to be related to maturity of concept formation. Draw-a-Man I. Q. scores averaged 4 points higher than Kuhlmann I. Q's. Product-moment correlation of these two intelligence measures was 0.73. This very high correlation indicates that the specific skills called for in the drawing test were not more radically affected in these cases of lead encephalopathy than was the general level of verbal and performance skills.

Distractibility and poor attention span, found pathological at first test, were noticeably improved at retest. Seven children were less distractible and could maintain attention for greater spans at retest. Four others were classed in the same category as at first test, and three became worse. Table 6 shows ratings on the same children for both years.

Social and Emotional Behavior

As indicated in Table 5, the emotional stability of these children deteriorated seriously at the time of the severe phase of lead poisoning. This would be expected in almost any serious illness. But here recovery was slower. Even eight months after release from the hospital 8 of the 15 children were still more prone to tantrums, crying, and fearful withdrawal than prior to illness. Of the 14 children seen 15 months later, at retest, 7 were found improved in these factors, 4 rated the same, and 3 rated more poorly.‡ It must be remembered that these ratings were necessarily subjective interpretations based on psychologist's observations, as well as on parents' descriptions of incidents. Although there is some element of unreliability in the ratings, the trend of improvement seems real. There was a different quality of ego function, of controlled drive and purpose, noted in the behavior of many of these children at retest.

TABLE 6.—*Distractibility Scale*

		No. of Cases	
		Test	Retest
Minimal	Completely absorbed by task	0	0
Low	Little interference from distracting stimuli	0	2
Average	Outside stimuli do not impair efficiency	1	5
Great	Easily distracted by extraneous stimuli or by own ideas but returns readily to task	7	4
Extreme	Abstracted, difficult to get and hold attention	7	3
		15	14

In their social relations to playmates, siblings, and parents, these children seemed to be doing better as a group. This may have been due in part to parents giving greater supervision of play activities, perhaps in part to siblings and playmates working out a different adjustment to the patient's aggressiveness (reported at first test), and perhaps in part to improved emotional adjustment of the patients themselves. Biting had become a less prominent behavior. Only 6 children bit at retest, whereas 10 did so formerly. Only one child, instead of the previous four, continued to bite other children. Fighting was also reduced.

Pica and Eating Habits

Pica, the habit which originally led to the poisoning and which could bring on a recurrence, had ceased in eight cases but continued occasionally in six. This incidence was about the same as that which prevailed 15 months before at the original examination. Most of the children avoided the lead-containing substances that caused their original illness; yet even the occasional ingestion of nonfood substances gives cause for concern. The younger sister of one patient was reported to have started the pica habit. All parents were again warned about the danger of this habit and urged to remove all possible sources of lead from the home. Since all the families are renters, they cannot do much to improve their flats; neither can they afford to move to better quarters.

‡ This report is a tabulation of *change* in behavior between test and retest. Table 5 reports the status of the children on the same variable at three different times.

Some are keeping the child out of the room or rooms that have peeling lead paints. The food preferences and dislikes, which at first test were not significantly different from average children of this age, had not generally changed in the ensuing 15 months. In five cases there appeared some increased fondness for sweets, but this was not consistent for the group. On the whole, our sample did not support any suggestion that pica is related to dietary factors.

TABLE 7.—*Pica Behavior*

	1953	1954	1955
No pica	...	7	8
Occasional or specific	...	5	5
Frequent and general pica	15	3	1
	15	15	14

Summary

Forty-six children were hospitalized with chronic lead poisoning in Chicago in 1953 and 1954. All the severe attacks occurred in summer. These children were mostly from very poor families. All showed pica. Dried paint was usually the noxious substance ingested. Most children had a characteristic premonitory syndrome followed by a severe stage, which included coma and encephalopathy.

Thirteen children died. The surviving 33 were studied psychologically, and 27 were found mentally retarded. In 20 of these the retardation was directly traceable to lead poisoning. One case could not be followed. Only 5 of the 46 children were alive and of normal intelligence. Speech was impaired in 18 cases. In addition to mental retardation, most children developed emotional instability and became very distractible. Some had behavior problems before their poisoning.

Two years after their illnesses 14 of these children were tested a second time. The second year of convalescence was one of recovery in some of the cases (less than half). Yet the trend was not complete enough to warrant optimism. Prevention of lead poisoning is the only adequate solution.

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Psychic Function of Temporal Lobe as Inferred from Seizure Phenomena

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Because seizure phenomena, especially when they arise from abnormal activity of discrete areas of the brain, display in isolation individual functions of the cerebral cortex, whether by activation or obliteration, they can be used to obtain information about the nature of cortical function. Hughlings Jackson, by careful observation and clear thinking, was able to infer not only the nature of motor and sensory functions of the cortex but also roughly to outline the motor and sensory homunculi. When he dealt with temporal lobe phenomena, however, his technique of inferring spatial arrangement on the basis of sequence of seizure phenomena failed, possibly because the gray structures of the temporal lobes are distributed in a more complicated spatial and functional arrangement than the cerebral cortex elsewhere. Also, Hughlings Jackson's efforts anteceded the development of psychodynamic concepts, and purely phenomenologic observations could not be closely related to the psychic life. The latter limitation, namely, dealing only with phenomenology and ignoring psychodynamic concepts, Penfield and Jasper imposed on themselves, too. Their much finer techniques made more illuminating observations possible and permitted them to go further than Hughlings Jackson. Nevertheless, the attempt to reconstruct psychic function without the use of dynamic formulation seriously limited their progress. It is the ambitious purpose of this paper to attempt to outline the psychic function of the temporal lobe primarily on the basis of an analysis of temporal lobe seizure phenomena, but utilizing psychodynamic concepts to fill in the gaps and provide a general frame of reference.

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One of the commonest temporal lobe seizure phenomena, whether spontaneous or evoked, is illusionary distortion of sensation. The illusions may be spatial, e. g., size (macropsia, micropsia), distance (near as opposed to far), or concerned with time (speed, recency), intensity (vividness, loudness), quality (pitch, color, texture), or clarity (sharpness, as opposed to blurred or muffled). In addition to these special sensory attributes which are subject to distortion in temporal lobe seizures, there are other attributes which may be similarly disturbed, though they are not ordinarily thought of as sensory qualities: (1) sense of familiarity, e. g., déjà vu, déjà entendu, déjà pensé; (2) sense of reality of the self, defect of which results in depersonalization, and (3) affective quality, that is, pleasantness or unpleasantness.

Let us direct our interest for a while to the first group of sensory qualities. If disease of the temporal lobe results in subjective distortion of these qualities, it is safe to infer that the temporal lobe is normally concerned with the perception of these qualities. Is there anything specific about these qualities which would account for their being grouped together anatomically? Why, for example, should not such visual qualities as size and distance be associated with other visual qualities, such as shape and pattern, rather than with auditory qualities, such as pitch and volume? Similarly, why should not these auditory qualities be associated with other auditory qualities, such as sound pattern (e. g., verbal or melodic), rather than with the above-mentioned qualities?

The answer to these questions is to be found, I believe, in a psychologic question posed a few years ago by Warren McCulloch: How does the brain perceive universals? In other words, McCulloch asked how it is that, although chairs differ from one another in size, color, proportion, location, and so on, yet any given chair is recognized as such, no matter what the details of its construction and location. A similar question may be asked about the sound of a word, which may be recognized despite wide differences in pitch, timbre, pronunciation, enunciation, and so on. McCulloch's answer was that the perceiving cortex is so organized that it attends only to pattern and not to accidental, irrelevant parameters of time and space. Specifically, he proposed a scanning mechanism, operating at alpha frequency, which performed this function of abstracting essential pattern from accidental irrelevancies. The evidence he proposed was suggestive but far from conclusive, and some recent work has failed to confirm the hypothesis.

One difficulty arises immediately: If it is indeed true that in the very process of perception, essential pattern has been separated from accidental detail, then too much information has been lost. While the recognition of the pattern is important, the accidental data of size, position, location, and so on, are also important for purposes of orientation, so that the proposed mechanism for recognizing pattern must also make provision for perceiving and recording accidental parameters.

I can offer no suggestion about the type of neural network or neural process by which this task is accomplished, and I should not be surprised if McCulloch's suggestion about a scanning technique should prove correct. However, on a grosser level, I think that McCulloch's question, How does the brain perceive universals?, can be answered as follows. In the temporal lobe there is a mechanism that divides any perception into essential pattern and accidental parameters, so that the two sets of data may be used independently. For this reason, focal temporal lobe seizures may evoke illusions limited to those sensory qualities that have to do with these accidental parameters. The illusions may be "positive" when there is ictal stimulation of the mechanism, yielding an exaggeration of a given quality, such as the sense of time or of space; or they may be "negative" when there is ictal paralysis of the mechanism, resulting in a loss of sense of time or space.

Let us now consider another temporal lobe seizure phenomenon, namely, the phenomenon which Hughlings Jackson called "mental diplopia" and of which Penfield speaks as "doubling of consciousness." Under the influence of this effect, the patient suffers some sensory aberration which he cannot exclude from consciousness, and yet he remains conscious of the fact that his subjective world is seriously distorted. In other words, his consciousness is pathologically altered, but at the same time (or alternately) he realizes that this pathologic alteration exists. The alteration of consciousness may be a sensory illusion, a simple hallucination, or the subjective impression of observing or participating in a dream-like fantasy. Essentially, there are two states of consciousness, one of which is automatic and irrational in the sense that the patient has no control over it and assumes no responsibility for it; and the other of which seems to be a rational observer with whom the patient eagerly identifies "himself."

Now this phenomenon resembles phenomena which may occur under circumstances other than temporal lobe seizures. It has some resemblance to the common experience of introspection. The difference is that in introspection the subject, while perhaps observing himself critically, will still not deny that the personality observed is his own, for which he is responsible, and of which he retains control. There are other nonpathologic circumstances in which this doubling of consciousness occurs. It is seen, for example, fairly commonly in the hypnagogic phenomena of dozing and awaking, and

often in dream phenomena. There are also normal instances of feelings of depersonalization.

In schizophrenia there is often an impression of a sensing and also of an observing personality. In this situation, however, the patient apparently is not aware of the pathologic nature of the aberrant sensations and identifies with that element which entertains these sensations. The observing personality, which is often more objective, and therefore critical of the pathologic personality, is considered to be another person entirely, and the image of this observer is fused with the image of the fantasied persecutor. However, this fusion should not obscure the "mental diplopia," though the latter might seem to be only one aspect of the paranoia.

In essence, in temporal lobe seizures and in some schizophrenic conditions, two separate conscious elements appear. Of these, one is subject to irrelevant, irrational impressions, and the second critically observes the first. In temporal lobe seizures the speaker identifies with the criticizing element of the personality, whereas in schizophrenia he identifies with the element which is possessed of the aberrant sensations.

Any functional disorder which results from a disease process may reflect, and thereby illuminate, an aspect of normal physiology. If one functional disorder appears in two or more disease processes, it bears close scrutiny as a presumptive clue to physiology. What can we learn about physiology from this phenomenon of "mental diplopia"? When a disease process results in a splitting, it often happens that the split occurs along a line of antecedent fusion. Jackson's term "mental diplopia" suggests that the doubling effect is caused by the separation of two phenomena which are usually seen as a unit because they are superimposed. How seriously can we take this analogy? One difference presents itself immediately. In the case of binocular vision, the two images that are superimposed resemble each other quite closely, so that when the images are separated the subject believes that he sees not two images but merely a doubling of a single image. In each of the two kinds of "mental diplopia" which we are now considering, the two "images," or types of subjective sensation, are quite different one from the other. Could it nevertheless be true that these images are normally fused, and that, in the two disease processes mentioned, they separate, so that both present to consciousness simultaneously or alternately? If so, what are the two elements fused, and what are the nature and purpose of the fusion?

Although we are not able to ascertain merely from the material so far available whether such fusion actually occurs, we may recall that the mechanism discussed above for abstracting accidental parameters from essential pattern would be necessary to permit any fusion which is based on pattern. That is to say, if two similar patterns are to be fused—or if any two patterns are to be matched for similarity and potential fusion—their images must first be adjusted in all nonessential respects; the images must be brought to the same size, intensity, clarity, and so on. Therefore, if sensory fusion occurs in the temporal lobe, it may be the function of this parameter-adjusting mechanism to facilitate it.

But what are the two patterns which are to be fused? One of the two personality segments which we have discussed seems to be occupied with an objective picture of the presenting environment. The other, in the fully developed psychic seizure, as well as in schizophrenia, seems to be occupied with specific, recurrent fantasies, some of which may be based on actual memories. The existence of these memories and fantasies in temporal lobe seizure phenomena led Penfield to suggest that they were there to serve as patterns with which current experience could be compared. However, the fantasies are so bizarre and the memories so unrepresentative that it is difficult to imagine how they could serve as the building blocks of behavior, or why these specific notions should have been selected for this service.

A conviction of reality attends the consciousness with which the speaker identifies, that is, the objective-observing element in temporal lobe seizures and the fantasy element in schizophrenia.

One of the most striking of the temporal lobe seizure phenomena is the automatism. The patient, showing no evidence of awareness of his real environment, attempts to carry out some procedure which is known to him, and from which he cannot be dissuaded. He deals with interference in a mechanical way, ignoring all remarks addressed to him. (Note that the perceptive apparatus is intact but intently selective.) The procedure itself is stereotyped, changing little, if at all, from one seizure to the next. (When the seizures are due to a progressive lesion, such as neoplasm, so that the site of the ictogenic focus changes, or when there are multiple foci, there may be several different types of seizures and more than one pattern of antomatism.) During automatism, the self-observing element which maintains contact with the real environment is absent, except perhaps momentarily at the start. Following the seizure there is no memory of it except possibly for a fragment at the beginning, before the self-observing element is obliterated. The actual procedure which is carried out is thoroughly irrational and usually shows no evident relation to the patient's real interests. In this respect it resembles the sensory fantasies. However, it seems to differ from the sensory fantasies in an interesting respect. Whereas the latter often show the subject participating in some activity with, or approaching, another person in the automatism, the subject either leaves on some solitary pursuit or fights with any person whom he selects for his object. In other words, automatism fairly consistently shows a separating tendency. This tendency is not consistently seen in the confused behavior (often called "automatic") which follows a seizure or results from intoxication or diffuse brain disease. During such confusion a definite approaching tendency (e. g., erotic invitations and gestures) is seen about as often as a separating tendency. Another noteworthy difference between temporal lobe fantasies and automatisms is that, whereas in the fantasies there are few situations which are openly sexual or aggressive, during an automatism solitary genital play and exposure and hostile attack are not unusual. It is difficult to know whether there is affect during the antomatism, since, although the patient seems quite strongly motivated, he can recall no conscious affect in retrospect.

Let us next consider the conditions of appearance of affect in temporal lobe seizures. We can make two generalizations. The first is that affect appears either alone or along with a fantasy. When it accompanies a fantasy, it develops during the evolution of fantasy, becoming strongest toward the end. It never precedes a fantasy. The second generalization is that the affect is almost always unpleasant. It will be recalled that the olfactory hallucinations which are often prominent elements in temporal lobe seizures are also almost always unpleasant. Since, of all the senses, the sense of smell is most strongly affectively charged, it is probably more than a coincidence that the affective polarity (i. e., unpleasant as opposed to pleasant) is similar in the two instances. (Moreover, we may be encouraged to speculate that, since in primitive vertebrates the olfactory sense is the sole or principal mode of exploration of the environment for instinctual gratification, in more advanced vertebrates the affect abstracted from the odor and based upon distance perception rather than contact stimulation becomes the new test for promise of gratification or threat.)

In summary, then, from examining the several elements and aspects of temporal lobe seizures, we have been able to make the following guesses: The temporal lobe is concerned with apperception, that is, with the interpretation of perceptions. In the performance of its function it employs two kinds of consciousness. One forms a realistic impression of the environment and the individual's role in it. The second seems

to be concerned with bizarre, unaccountable fantasies, having no relevance to the environmental situation and apparently derived solely from internal sources. The first carries a conviction of reality, and the second has the power of evoking affect. There is a device which corrects for accidental attributes, leaving pattern unchanged, so that the images derived from the two sources can be fused. If fusion is successful, the resultant picture should carry both a conviction of reality and an affect. Since, in temporal lobe seizures the affect is unpleasant, it seems to put an end to the fantasy which generated it. The temporal lobe can also activate behavior which is seemingly purposeful, but during the behavior the patient cannot communicate his awareness of any consciousness, nor can he remember afterward whether any existed during the automatism. Moreover, this behavior shows a consistent separative tendency. It seems to me that this is as far as one can go with examining the phenomena of temporal lobe seizures and a priori reasoning about them.

It will be fairly obvious that we have been dealing here with concepts which strongly suggest fairly classical psychoanalytic formulations and some of their corollaries. Since this is a paper about seizures, not about metapsychology, I shall not embark upon a review of the psychology of apperception but shall attempt merely to use metapsychologic theory to fill in the gaps left in our discussion and to outline a frame of reference for it.

Let us consider first the faculty of abstracting essential pattern from its background of accidental parameters. In the framework of instinct theory, the essential patterns that require recognition are the pattern of the object of instinctual gratification (e. g., parent, sexual object) and the pattern of the contact apparatus (e. g., breast, mouth, genitals). The exquisite specificity of these instinct-releasing patterns has been demonstrated by students of animal behavior. Moreover, extirpation of temporal lobes of monkeys, cats, and other mammals (Klüver and Bucy, Schreiner and Kling) has been found to result in loss of the faculty of discriminating recognition of these patterns of object and contact apparatus (though not of the faculty of using them pleasurably, once contact has been made). While the recognition of patterns is essential to determine whether any given environmental presentation promises gratification or threatens harm, one must also assess and record the accidental parameters in order to judge the likelihood of consummation and the appropriate technique for achieving consummation.

Is there in metapsychologic theory a place for the fusion process we have been led to infer? Let me quote from Nunberg:

> An actual perception of an idea revives old, unconscious, repressed ideas or emotions to such an extent that they are perceived as actual images although their meaning is not recognized by the conscious psychic apparatus; thus present and old ideas and emotions become identical for a while. . . . An actual event reactivates an old repressed one which, on its part, tries to replace the new experience. . . . It seems as if a new experience could not be assimilated . . . unless it found its way to the old patterns.

In other words, according to psychoanalytic theory, apperception proceeds by the superimposition of the perception of the external data upon some idea or memory which has independently no access to consciousness. This unconscious idea contributes an affect to the apperceptive experience. Here, then, we have the psychologic basis of the fusion we were led to assume from phenomenologic analysis.

But we have more than we expected. Not only do we have a confirmation of our own inferences, but we have a suggestion for the solution of a problem which baffled us. It will be recalled that we could not account for the bizarre, irrelevant fantasies that appeared in temporal lobe seizures or why they should constitute one of the two elements of the fusion process. Notice that psychoanalytic theory identifies the second element of the fusion as an unconscious idea. Yet the irrational fantasies of temporal lobe seizures are not unconscious, for they are

often memories which have access to consciousness even in the absence of seizures. There seems to be some discrepancy here—but it is only apparent, and it arises from an omission in my statement of the psychoanalytic formulation. If an idea is unconscious, that is, has no access to consciousness, how can it influence the conscious life? It selects from the multitude of experiences which crowd upon the individual a few which express the same tendency or goal (or use the same instinctual technique) as the repressed tendency. Upon these few, the unconscious idea confers a forcefulness, vividness, and persistence, as well as a tendency to repeat itself, which the experience or its memory per se does not deserve. In other words, what may be an unimportant or even bizarre idea becomes a powerful tendency which seeks to impose its pattern upon perceptions and actions by virtue of its representing an unconscious idea. Such conscious ideas which represent and express unconscious ideas are called derivatives. Therefore a fuller statement of the metapsychology of apperception would read as follows: Current perceptions are superimposed upon, or compared with, unconscious ideas by being fused with conscious or unconscious derivatives of these unconscious ideas. It is now clear that the mysterious second bizarre element of the fusion in apperception is a derivative of the unconscious idea, in the light of which the current perception is being judged.

Let me illustrate. A young woman was worried that she would neglect or injure her newborn son when she would assume full responsibility for his care. Analysis disclosed that she had wished to kill her brother when she was a child. She had thought during the past few days that her son resembled her brother. How was this wish to kill transferred from the brother to the son? The vulnerability of the little child, and the fact that he, his equipment, and his nurse preempted a large portion of her small apartment, reevoked the long repressed wish originally directed against her brother. Now when she looked at her son, she felt and acted as though she had seen her brother. In fact, it seemed to her that her son looked like her brother, although no one else had observed such a resemblance, nor had she previously. We may say what she saw when she looked at her son was actually a condensation of the images of her son and her brother as a baby. The percept of the son conveyed to the vision or the apperceptive its form, and a sense of reality, while the memory image of the little brother contributed the childhood wish and the affect of guilt.

It also becomes clear that the affect which regularly constitutes an essential element in apperception is the affect which applies to the unconscious idea and which therefore attends its derivatives. This is the affect which appears in temporal lobe seizures with the evolution of the fantasies. It is by this affect that the current perception is judged to be either welcome or unwelcome. Since the affects which appear in temporal lobe seizures are unpleasant, one may speculate that the temporal lobe apperceptive mechanism is asked to judge, not whether a given perception promises gratification, but whether the perception which promises gratification may not also be a threat which must therefore be avoided rather than approached. Patterns of avoidance, in psychoanalytic terminology, are called defenses. They consist of manifestations of flight, belligerence, solitary activity, or shift of interest. I believe that most temporal lobe automatisms can be subsumed under this category of activity. Why the fantasies should remain mental while the automatisms are acted out is not clear except that the apperceptive judgments in which the fantasies participate are normally purely mental activities, whereas the defensive attitudes to which they give rise are usually carried into action.

In summary, I have tried to demonstrate that from the phenomena of temporal lobe

seizures one can infer that the psychic function of the temporal lobe is the formation of apperceptive judgments, especially negative ones. This task is accomplished by the fusion of the current perception with a memory. This formulation corresponds quite closely with the psychoanalytic description of the process of fusion of current perception with the derivative of an unconscious idea, so that the affect attending the unconscious idea and its derivative colors the apperception.

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Some Observations on the Use of Tranquilizing Drugs

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The widespread acceptance and use of the so-called tranquilizing drugs constitutes one of the most noteworthy events in the recent history of psychiatry. This development is being hailed in many quarters as the beginning of a new era in psychiatry and "mental health." Even when these drugs are not claimed to "cure" the patient, it is asserted that their use makes him more amenable to other forms of "therapy," either within the hospital or outside. The purpose of this essay is not to evaluate the effects of these drugs on behavior. We accept as a premise (without, however, necessarily subscribing to it) that the pharmacological agents under consideration (chlorpromazine, reserpine, etc.) do indeed bring about the behavioral changes currently ascribed to them.[1-3] What I wish to comment on, rather, is the *social fact* that these drugs are used. This event itself can rightly be made the subject of scientific inquiry. Indeed, such an inquiry would seem to be desirable to counterbalance and complement an otherwise one-sided enthusiasm and optimism about this novel aspect of psychiatry. No detailed exposition of the sociopsychological aspects of psychopharmacology as therapy will be attempted here. I shall confine myself to sketching briefly some of the considerations which arise in connection with a contemplation of this subject. These may be conveniently organized around the following three questions: 1. What do we, as physicians and psychiatrists, do when we prescribe these drugs? 2. Whom do we treat? 3. Is what we do right (just)?

Some—or perhaps many—will undoubtedly disagree with my suggestions about how best to answer these questions. Be that as it may, I think all will, or should, agree that raising such questions, and thinking about them, is the duty of all thoughtful men faced with measures of such far-reaching medical and social implications.

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Does Psychiatry Deal with "Mental Illness"?

Modern psychiatric thought is influenced by and reflects chiefly two sources of knowledge. One of these is medicine, including its basic sciences, such as chemistry, physics, biology, and pharmacology; the other source in sociology, psychology, anthropology, philosophy, semantics, and other disciplines dealing with experience, symbolism, and behavior. Some schools of psychiatric thought lean more heavily on one, and some on the other, of these two metaphorical "parents" of psychiatry (e. g., psychosurgery and psychotherapy and their respective theories). Still others try to combine what they consider the best features of both (e. g., psychoanalysis, "neuropsychiatry," etc.). The result is that there exists a much greater "hodgepodge" of methods and concepts in psychiatry than in most other branches of medicine.

Conceptually, the use of tranquilizing drugs rests on the medical model of "disease." In this context we deal with two principal notions, namely, "disease" and "symptom" (or "sign"). Thus, pneumonia is a disease; chest pain, cough, fever, and leukocytosis are its symptoms and signs. Similarly, we hear speculations about whether the drugs in question "cure mental illness" or whether they only control its "symptoms." Most investigators claim no more than symptomatic control. The abolition of anxiety, tension, restlessness, and

combative behavior are thus regarded as analogous to the control of pain, discomfort, and excessive fever by acetylsalicylic acid in an infectious illness. The implication of all this, of course, is that, while we do not yet have penicillin which will *cure the disease*, we might achieve such a result by dint of perseverance, and thus "cure mental illness." If, by the way of comparison, I may be permitted to cite a somewhat inelegant example of this sort of program, I would recall a slogan which was popular in the early days of Nazi Germany. It was: "Today we conquer Germany—tomorrow the whole world." In medicine, first we are satisfied with mastering (controlling) symptoms; later we hope we shall be able to do the same with the disease. The history of bacteriology and the control of infectious diseases shows that this can be done. In view of this, what possible objection can there be to an analogous pharmacological approach to "mental illness"?

The objection, of course, is a familiar one and consists of the possibility that the things which we now call "mental illnesses" are not "diseases" at all. In other words, suppose that the model of "disease-and-symptom" does not apply to the phenomena under study. If such should prove to be the case, we would, at best, be wasting our time, and, at worst, be damaging our patients and society.

This is not the place to consider the evidence for or against the view which regards psychiatric disorder as "mental illness."[4] While it is popular nowadays to speak of "mental illness," many psychiatric investigators have found that the psychological and social approach to behavioral phenomena greatly limits the relevance and value of this conceptual model. A moment's reflection will show that our present custom of considering everything (and human behavior does encompass almost everything*) to which a physician addresses himself as "disease" is no more rational and useful than considering all sorts of diverse happenings in terms of economic, political, or religious concepts. Similarly, we persist in calling all that transpires between physician and patient "treatment," no matter how disparate these phenomena might be, and even disregarding whether or not the "treatment" helps the patient. Szasz and Hollender[6] have called attention to three major categories within the broad concept of "disease." They noted that each different concept of "disease" carries with it its particular view of "treatment" and "cure." Moreover, historical and scientific change often leads to changing concepts of "disease." For example, what in one era was regarded as "disease" became the "symptom" of the next scientific epoch, and so on. Not long ago, fever was an "illness," and its disappearance was "cure." Today tuberculosis, malaria, and typhoid are still widely regarded as "diseases." At the same time, we are also at ease with another view of these disorders, according to which they are "symptoms" of certain social (economic, public health, etc.) conditions. These examples are trivial and are cited only to remind us that "disease" is not an impersonal, objectively given "entity"—which "exists" in nature and waits for man's discovery of it—but, rather, that it is a concept which we *make* as we go along in the exploration of our experiences.

Philosophical Problems Raised by Use of Tranquilizing Drugs

Let us turn our attention now to the three questions mentioned at the beginning of this essay. I shall briefly indicate the generally accepted, that is, official or "scientific," answer to each of the questions. These will be supplemented by some considerations which are recommended as further, perhaps more appropriate, "explanations" for the phenomena at hand.

1. What do we, as physicians and psychiatrists, do when we prescribe tranquilizing drugs? The commonly accepted answers include the following: We treat the patient's

* "Psychology . . . is an essential ingredient in every part of empirical science."[5]

"symptoms," such as tension, agitation, and combativeness, which are manifestations of his "mental illness." We make the patient more tractable and therefore more amenable to hospital management or auxiliary "therapy" as an outpatient. We relieve the acutely disturbing manifestations of a behavioral disturbance, and this might lead to a readjustment of the whole person ("cure").

2. Whom do we treat? This question might sound trivial but it is not. It is inherent in the foregoing comments that we treat the "patient." Yet it is equally obvious, and often explicitly stated, that these drugs make the disturbed hospitalized patient more manageable (i. e., less disturbing to ward personnel and other patients). Accordingly, we also treat the hospital staff and patients other than those who receive the drug.

3. Is this form of treatment justifiable, or, in other words, is it right? Obviously, the answer must be yes; otherwise, it would not be generally accepted practice. This is the nomative concept of "right" as used in jurisprudence in a democratic society. Yet we know that patterns of behavior—whether pertaining to medical practice or to political conduct—generally approved at one time may be looked upon in quite another light at a later time. This alone commands caution against the ready equation of statistical frequency with "rightfulness."

Now we turn to the objections to the foregoing "explanations" and the consideration of other possibilities. The following comments rest, of course, on the assumption that so-called psychiatric disorders do not lend themselves to fruitful analysis and management in terms of the medical model of "disease-and-symptom." For our present purposes we prefer to regard them in sociologic terms as deviant forms of behavior, and in psychologic terms as "conflicts" and attempted "solutions" of conflicts. While it may be objected that the psychosocial aspects of mental retardation, senile psychoses, psychoses with metabolic or endocrine disease, and many other types of "psychiatric disorder" do (or may) lend themselves to fruitful understanding and treatment in terms of the traditional medical model, the possibility still remains that the majority of the so-called "functional psychoses" will have to be approached differently. Be that as it may, I wish to make explicit that this essay rests on the latter assumption but it does not imply that all "psychiatric disorders" (now so called) can be relevantly dealt with in terms of "conflicts."

Is it not possible that the use of these drugs represents a modern version of the "furor therapeuticus"—a traditional "occupational disease" of the physician? The last several decades have brought us, in rapid succession, various forms of "shock treatments," psychosurgery, and, lastly, the tranquilizing drugs. All have in common the fact that they provide socially sanctioned patterns of medical action and thus help the physician to do something when he is faced with a psychiatric problem. (It is not implied in this context that these methods are not helpful but that psychotherapy is!)

The answers to the second question ("Whom do we treat?") might be implemented as follows: We treat ourselves. This possibility must—I submit—be considered in all forms of treatment. Furthermore, we treat the patient's environment, in the widest sense of this word (family, hospital staff, other patients, society at large, etc.). This claim is supported by the "fact" commonly agreed upon, that the chief alterations in the patient produced by these drugs pertain to making his behavior more socially acceptable. These drugs, in essence, function as chemical strait jackets. The restraint of patients who annoy society is, of course, a time-honored procedure. What is significant in this context, however, is the possible confusion of motives, actions, and results. In other words, when a "disturbed" patient is forcibly restrained, it is clear that this serves the protection of those about him and of the community at large. It may or may not be also "helpful," in the long run, to the patient himself. When a similar

effect is accomplished by chemical means, it is much easier to mistake the process for "treatment," the primary aim of which is to "help the patient."

The foregoing considerations lead directly into our third question ("Is it right to treat patients this way?"). The more we consider the complexity of this matter, the more dubious it becomes whether or not this mode of treatment is justifiable. To me, it seems hardly right to emphasize that these drugs "help the patient," inasmuch as it is more apparent that they help others (e. g., like the segregation and confinement of patients with leprosy).

Deviance and Rebellion in "Mental Illness"

The foregoing words of caution imply criticism. Criticism is rarely welcome and is often particularly resented when the critic has, so to speak, nothing better to offer than that which he criticizes. This all too human reaction to criticism has probably played a role in stimulating the advocates of psychotherapy to claim more for this mode of influencing people than can be readily substantiated. While I am personally impressed by the role of psychological and social forces in human relationship, I definitely want to avoid casting this essay into the framework of physiological versus psychological forms of therapy in psychiatry. It seems to me that words of caution and criticism—when appropriate—must stand on their own feet. The suggestion of better alternatives is desirable but is really another matter altogether. (No one expects a drama-critic to write a better play than the one on which he comments. Similarly, the inadequacy of a scientific hypothesis may be demonstrated without necessarily suggesting a better one. Why should it be otherwise in the case of therapeutic techniques?)

With this premise in mind, I shall sketch briefly a conceptual model of psychiatric disorders which is different than the one which has been criticized. This model is not novel, since it is held by many psychiatrists. It will be restated here—perhaps greatly oversimplified—not in order to acquaint any one with this aspect of psychiatric theory but only as background information to substantiate and clarify the doubts which have been raised about the use of tranquilizing drugs.

Most so-called psychiatric conditions, such as schizophrenia, depression, alcoholism, and so forth, show us the individual in conflict either with specific individuals or with society as a whole. It is fundamental to our understanding of problems of mental health that, on the whole (sociologically speaking), compliant behavior tends to be viewed as normal and deviant behavior as abnormal. In all "mental illness" (we use this word, without subscribing to its misleading connotations, only for ease of communication) the patient vacillates between compliance with and defiance of parental—and later social—commands and expectations. Often this problem leaves society relatively uninvolved, especially when the person experiences the wishes to submit or rebel primarily in relation to his own inner images of his parents and their substitutes. In patients with schizophrenic and other disturbances—who make up the population of mental hospitals and who are the potential candidates for tranquilizing drug therapy—we invariably see the individual in some degree of overt (social) conflict with those about him. The so-called "disturbed" patient may or may not be "disturbed" in terms of his own feelings. The term reflects more accurately the fact that he disturbs others. This, among other things, is what we mean by deviant behavior.

An analogy may be drawn to the model of an infectious disease. We view such a disorder as a sort of battle between the organism, on the one hand, and the microbes, on the other. The microbe is an "enemy" (within); here we lean on the metaphor of nations engaged in warfare.[7] Similarly, we might picture "mental illness" as revolving around the theme of a battle between the patient's own sense of identity,

on the one hand, and those whom he feels thwart his needs and endanger his survival.[8] The original adversaries are usually his parents. Later others in authority may take this role, as, for example, physicians, or often "society" as a whole. Assuming that such a battle is indeed what happens, and that what we call "mental illness" is a manifestation of it, what alternatives for interference in this process are open to us? Again, with due allowances for oversimplification, the following three basic modes of action present themselves: 1. To interfere as little as possible in the patient's life and let him "work out" the conflicts as he sees fit. The minimum interference ("treatment") would have to include making sure that the patient does not seriously injure himself or any one else, (e. g., humane confinement).[9] 2. To concentrate on separating the "combatants." This takes place when patients are forcibly restricted to institutions and are otherwise segregated from society. This casts society into the aggressive and damaging role in which it has already been conceived by the patient. It makes the "working out" of the conflict more difficult. As a rule, this arrangement leads to the permanent defeat of the patient and the victory of the forces of society (at a certain price to the latter, which it is willing, however, to pay). 3. Lastly, to employ sanctions against the patient in an effort to make him conform to the demands of society (parents). Shock therapy, lobotomy—and other measures collectively, and with good reason, called the "drastic therapies"—might be viewed as doing just this. The use of tranquilizing drugs belongs in this category.† In a similar context, Meerloo aptly spoke of "medication into submission."[10]

By approaching the problem of "mental illness" in terms of a conflict between the patient and other people (or, broadly, society), we are better able to clarify certain questions about whether the tranquilizing drugs constitute good therapy and whether their use is morally justifiable. In most medical situations the patient does not present the physician with the dilemma of helping him and hurting society, or vice versa. Apparently, in some psychiatric situations he does just this. Physicians have been proud, and justly so, that they have eliminated, to a very large extent, the element of moral judgment from their daily work. If a patient has a broken bone, the physician will set it whether he be sinner or saint. Unfortunately, however useful this model of the physician's role may have been in the past, it appears that we must now modify it or give it up in psychiatry.

Accordingly, physicians will have to clarify the effects of their ministrations in behavioral disorders. They will have to be clearer than heretofore about whether they help the patient or others. Are they agents and representatives of the best interests of the patient, his relatives, the hospital, or society? What if these interests clash?

Without belaboring these issues further, it is clear, in summary, that (if our hypothesis is correct) the best interests of the patient necessitate the maximal recognition of his right for self-determination, growth, and the working out of conflicts. On the contrary, the greatest (immediate) protection of society may conceivably lie in the use of severely repressive measures against deviant citizens, whatever the cause of their behavior.

Yet it must be noted here that it is held by many that possibilities for defiance of authority and deviances from social norms—within certain clearly set limits—must remain open to the individual as a prerequisite for his "mental health," as well as for the well-being of a free, democratic, heterogeneous society. Thus, excessive sanctions against individuals manifesting deviant behavior might effectively protect society for a short period; its danger, for the long run,

† In this essay I have aimed only at an analysis of the use of tranquilizing drugs in situations which are formally recognized as "psychiatric." Accordingly, the observations and inferences presented either do not apply or apply only partially to the widespread prescription of these substances in general medical practice.

is that the protective measures themselves might bring about a transformation of the social structure such as was not desired by those who advocate the protective measures in question. Which "treatment" is justifiable and which is not will depend on the position which we take about these and similar questions. In any event, what is ethically "wrong" is to use a mode of "treatment" which benefits others than the patient and claim that it is for his welfare. It is in this connection that I see the gravest dangers in the use of tranquilizing drugs, and, for that matter, also of certain other forms of psychiatric treatment, including psychotherapy. In other words, when patients had to be restrained by the use of force—for example, by a strait jacket—it was difficult for those in charge of their care to convince themselves that they were acting altogether on behalf of the patient. The use of drugs (and of psychotherapy) removes the safeguards inherent in the guilt feelings of the therapist. Restraint by chemical means does not make us guilty; herein lies the danger to the patient.

Summary

The purpose of this essay is to inquire into, and call attention to, some sociopsychological aspects of the current vogue of using tranquilizing drugs in psychiatric disorders.

The use of these drugs rests on the premise that psychiatry deals with "mental illness" and that such illness presents a problem essentially analogous to that encountered in medicine (and particularly in infectious disease). There is evidence to suggest that this "medical" model of behavioral disturbance is inadequate and misleading. If such disturbances do not constitute "diseases" which manifest themselves in certain "signs" and "symptoms," then measures based on this concept are likely to be faulty, and probably harmful to patient, physician, or society.

A brief analysis of this problem is organized around the following three questions: 1. What do we, as physicians and psychiatrists, do when we prescribe tranquilizing drugs? 2. Whom do we treat? 3. Is this form of treatment justifiable? The generally accepted answers to each of these questions are summarized. They are followed by suggestions for additional possible "answers," the most important of which are (1) that the use of these drugs may represent a new "symptom" of the ancient occupational disease of physicians known as "furor therapeuticus"; (2) that we treat ourselves and the patient's social environment, and (3) that whether we hold the treatment to be justifiable or not will depend on what position we take vis-à-vis the patient's conflict with other persons and society.

In conclusion, the role and significance of defiance of authority and of deviance from social norms in "mental illness" (and in all modes of human life, for that matter) are briefly mentioned. These considerations are emphasized in an effort to substantiate the legitimacy, and possible value, of taking a position of caution and criticism with respect to the widespread use of tranquilizing drugs in medical and psychiatric practice.

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The Trouble with Psychiatric Research*

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To free the 728,000 patients in mental hospitals and to help the estimated 10,000,000 people in the United States who suffer from some kind of mental illness is one of the goals of psychiatric research.[39] But the road ahead seems long and the end nowhere in sight. The apparent absence of spectacular advances in the field of psychiatry has been variously blamed on lack of funds or on poorly trained or underpaid personnel. But there also exist other factors—more intangible and perhaps equally crucial—which can be traced to social structure, cultural values, and ways of living. Since these features have in common that they cannot be corrected by administrative and organizational means alone, a change in attitude of researchers, sponsors, officials, and the public at large is necessary before an atmosphere can emerge which will favor creative contributions. A brief review of the factors which interfere with psychiatric research might help to remedy some of these adverse conditions.

The Rate of Psychiatric Progress Is Slow

Old-fashioned methods and inadequate theories are largely responsible for the slow progress of psychiatry, which can be demonstrated by a comparison of present morbidity rates with those of 50 years ago. Goldhamer and Marshall,[19] in a careful statistical study, come to the conclusion that "first admission rates for ages under fifty are revealed to be just as high during the last half of the nineteenth century as they are today . . ." but "there has been a very marked increase in the age-specific admission rates in the older age groups." From these and other studies,[35,36] it becomes evident that except in neurosyphilis and pellagra research has not resulted in the development of any preventive methods which have significantly decreased the incidence of mental disease.

Some progress, however, is detectable in the duration of mental disease. The probability of release in the first year after admission for patients with functional psychoses was greater in 1946 than in 1916. "Indeed, now within one year after admission, more patients are released from the hospital than were released within five years during the earliest period."[27] However, the chances for discharge of those in their second or third year of hospitalization did not change. Unfortunately, it cannot be decided with certainty whether physical, psychological, or pharmaceutical measures are responsible for the more rapid release of patients or whether other factors, such as differences in the type of patient admitted, condition upon release, and the readiness of the community to accept the discharged patient, have brought about a turn for the better.

Few Physicians Are Engaged in Psychiatric Research

In 1942, the National Committee for Mental Hygiene[52] surveyed the field of psychiatric research and found that only 37 of 613 nongovernmental institutions professed to be doing any research and only 26 of 66 medical schools reported research activity related to psychiatry. Menninger, in 1949, wrote[33]:

> It is reasonable to assume that there are not a dozen full-time research workers in the field of psychiatry in the United States at the present time. This number would be slightly increased if we included those individuals who are working in clinical psychology.

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* Special article.

The shortage of psychiatric research workers with an M.D. degree has led to a peculiar and unfortunate situation. Much of the research in mental disease has been taken over by nonpsychiatrists, such as biochemists, pathologists, physiologists, psychologists, sociologists, anthropologists, and others. This trend comes clearly into evidence if one considers that the Mental Health Study Section of the Public Health Service, which passes on various applications for support of research in mental disease, is currently composed of eight M.D.'s and nine Ph.D.'s. Although research workers in the life sciences greatly advance knowledge in many directions, they rarely tackle the main issue of psychiatry, namely, abnormal behavior and experience. But as long as various circumstances seem to prevent psychiatrists from investigating the core problem of mental disease themselves, a lot of research irrelevant to psychiatry will be carried out under the flag of mental health.

In the Universities, the Professional Staff Is Underpaid

The shortage of psychiatrists engaged in research uniformly has been blamed on the poor pay. Indeed, it is true that inflation, taxes, and the increase in purchasing power of many occupational groups have changed the social and economic position of the full-time university research worker. In 1908 the top salary for a professor at the University of California was $5000; in 1953 it would have taken $19,200 to provide him with the same purchasing power.[47] Meanwhile, the purchasing power of workers in seven representative industries from 1904 to 1953 increased on an average of 130%. And while the purchasing power of professors in 120 state-supported institutions declined 24% from 1939 to 1953, the purchasing power of factory workers increased 43%.[18] Allowing the professor to participate in the increased productivity of the country as a whole would set his top salary at about $45,000. However, the actual top salary is $13,200.

Matters get even worse if one considers that young men do not get full professorial salaries. An assistant professor at the top level in the University of California now earns $7176. If he is married with two children, this sum is not even sufficient to maintain a reasonable living standard, which for a salaried junior professional today requires $8129.[54] But the young assistant professor also has to amortize over $30,000 which he spent on his 14 years of medical education,[11] comprising college, medical school, internship, and residency, until he is eligible for the Board examinations. Frequently such training includes a personal psychoanalysis. When he finally reaches the age of 31 or 32, perhaps adding another two years for military service, the $7176 he earns does not suffice to get him out of debt. If an institution attempts to retain him for teaching and research, he will bring forth the potent argument that, in spite of his age and training, his salary is less than the income of one of the shareholding garbage collectors in San Francisco.[48] No wonder that he does not stay. The scientist and professional working in research thus have been discriminated against, with the result that ambitious and talented young men will seek their fortunes outside the academic field. Writes Alan Gregg: "On the point of recruitment, I suggest to you that neither in quantity nor quality has psychiatry drawn from the medical schools the students appropriate to the nature and the urgency of its need."[21] And this, of course, is because the rewards in psychiatry do not compare with those available in other fields. Russia, in contrast, pays its professors compensation which is comparable to that of our industrial executives. Thus salaries of $50,000 and up are not uncommon.[55]

At present there is in America no opportunity for the top professionals in university employ to earn about the same amount of money as their colleagues in private practice or industry. Not even their prestige is comparable to that of the great money-makers. Unless equal rewards are available in various occupations to men of equal

ability, talent will be drained off into the more lucrative channel rather than being evenly distributed. A chain is as strong as its weakest link, and if an occupation like that of teacher, scientist, and research worker is neglected, the nation as a whole will eventually suffer. In wartime, the lack of trained scientists may even mean death to millions and the destruction of the nation. For a country as rich as the United States, the policy of neglecting higher education and the procurement of scientists approaches the suicidal.

Lack of Research Funds May Be a Crucial Factor

There are some experts who believe that if sufficient money were spent on research in psychiatry results would automatically be forthcoming. They point to the fact that of all the funds allocated for medical research only about 5% (1946-1951) is spent on mental health research.[13,14,49] Since, in terms of dollars and cents, the cost of mental disease to the nation is about $3,500,000,000 per year,[39] the $18,000,000 spent in the fiscal year 1955-1956 in the United States on psychiatric research above and beyond the regular university and hospital budgets seems to be but a drop in the bucket. But, although an increase in funds may enhance the chances for advances in the field of mental disease, it does not explain why the money expended so far has produced so few results—this particularly in view of the estimate that in the United States more money has been spent on psychiatric research than in all other countries combined, but the harvest, as it were, has been lower than in other Western nations.

One of the reasons for this low yield may be found in the present fashion trend to establish mammoth research studies. As soon as a group exceeds three or four people, it needs to establish its own control devices and its own bureaucracy, which, in turn, increases the cost of research. Although no accurate figures are available, it is safe to estimate that for every full-time person engaged actively in research one or more clerical or administrative persons operate behind the lines. This ratio seems to increase the larger the studies become. Thus, if the fund-giving agencies would distribute smaller amounts of money to a greater number of psychiatrists, they would increase productivity per dollar spent instead of swelling the already overcrowded ranks of bureaucracy.

Psychiatry Needs a New Theoretical Framework

In the behavioral disciplines there exist two distinctly different factions which hold opposing views concerning the nature of sociopsychological events. The proponents of psychiatry as a science are positivists who want to follow in the footsteps of physical science. Exponents of psychiatry as an art are subjectivists who maintain that ordinary scientific methods are entirely inapplicable to the data of behavior[41]; they believe that the physical scientist's method of splitting the universe into progressively smaller entities is a meaningless procedure when applied to behavior. Together with the Gestalt psychologists, they emphasize that comprehension of social and psychological phenomena and the understanding of human experience are based on the appreciation of patterns and that reduction, analysis, and isolation of elements destroy this patterning.[44]

Another significant difference pertains to the identity of the observed events. When the scientist deals with unidentified particles, he cares but for the mass effects; and since his presence hardly affects the events in question, he can remain objective. But when the observer deals with identified individuals and not with mass effects, not only does he influence what he observes but it influences him in return. Therefore his relationship is subjective. Many difficulties in psychiatric research thus can be traced to differing assumptions about the position and properties of the human observer. Obviously a unified theory of human behavior has to be

developed in which, in contrast to the schemes used in natural science, the observer is assigned a variable position within the system of which he is a part. Although the beginnings of such an undertaking are in the making,[23] at present not enough effort, time, and money have been devoted to a revamping of the theoretical framework of psychiatry.

Verbal Unreality Retards Psychiatric Progress

The peculiarities of language introduce a number of distortions into psychiatric research. When words are employed to refer to behavior, action and movement, which are continuous functions, are sliced into discrete elements, as if they were replaceable parts of a machine. The continuity of existence thus is split into arbitrary entities which are not so much a function of actual behavior as the result of language structure.

But splitting into part functions that which is whole is not the only sin of verbal language. Words enable us to telescope and condense natural and far-flung events as if they had happened at the same time and in the same place. This spatial and temporal distortion is particularly prominent when the psychiatrist talks about traits, attitudes, abilities, or other personality features. In the use of such concepts, the time-bound and situation-specific characteristics of experience are disregarded. By talking in generalities, we create such verbal monstrosities as "he is a liar," representing the person as though he were characterized by these features 24 hours a day throughout the year. Verbal reports of behavior thus contain so many distortions that they seriously handicap the work of the investigator.[46]

The distortions that language introduces do not concern the psychiatrist alone. Indeed, the world of verbal unreality is shared by all those professions which are built upon communication. Thus primarily among administrators, almost all politicians, psychotherapists, social scientists, and lawyers words tend to be treated as absolutes. The fact that words are sounds which refer to images and ideas and that these are products of the central nervous system is frequently lost sight of altogether. The act of speaking and writing, in the minds of the verbal professions, invests words with substance and body, as if they were something separate from the human being from which they originated. Just as technological development depended upon advances in the field of mathematics, so we can expect that the behavioral disciplines will progress when the recording of behavior will become more independent of words. At present, not enough research studies have been devoted to this methodological difficulty of psychiatry.

Search Rather Than Research Is Needed in Psychiatry

Investigative work technically can be divided into three categories: Basic research inquires into the processes involving man and nature in an attempt to evolve new general principles; applied research is concerned with the adaptation of basic rules and principles to specific problems; developmental research is directed at the perfection of methods and products that are already known. At present, psychiatric investigations fall mainly into the area of applied research.

Exploratory research, search in the unknown, or basic research can only be carried out successfully by universally trained people who are capable of dealing with problems even if they fall outside their particular field. Developmental research, or research with an emphasis on the syllable *re*, is an engineering task which, when the basic idea is known, is devoted to filling in the technical details.[50] Trained technicians with experience limited to one field are quite adequate for this kind of work, provided that another person coordinates the team. Thus, multidisciplinary research[43] is useful for applied and developmental research but not for the creation of novelty, which is the result of the efforts of one organism. At the moment, psychiatry is in need of people with ideas—searchers in the true sense of the word—who can open new vistas and

TABLE 1.—*Examples of Creative Ideas and Theories in Psychiatry*

Place	Name	Contribution
Vienna	Freud	Personality model based on relationship of forces
Zurich	Jung	Analytic psychology; psychopathology of schizophrenia
Zurich	Bleuler	Phenomenology of schizophrenia
Heidelberg	Kraepelin	System of psychiatry based on prognostic criteria
Tübinger	Kretschmer	Relationship of personality to body build and its prognostic implications
Paris	Janet	Survey of the various psychological healing methods and description of psychasthenia
Leningrad	Pavlov	Conditioned reflex theory
Washington	Sullivan	Interpersonal theory of psychiatry
Baltimore	Meyer*	Reaction types
Kreuzlingen (Switzerland)	Binswanger	Phenomenological psychiatry

* Swiss-born and educated.

bring forth new facts. Although it is obvious that the stagnation in psychiatric research can only be overcome if training efforts are directed toward the education of thinkers, planners, and explorers, some of the leaders in the field have been led astray by believing that neurophysiological and psychoanalytic knowledge was sufficiently advanced to justify the training of large numbers of practitioners and to steer investigations toward developmental and applied research. So far, neither the increased number of psychiatrists nor the emphasis on multidisciplinary investigations has materially changed the incidence or recurrence of mental disease.

In Psychiatry Most Original Ideas Are Imported from Europe

With the exception of Sullivan's interpersonal theory,[53] advances in theory and knowledge in the field of psychiatry have been contributed by Europeans[5,31] (Table 1). Likewise have all therapeutic methods used in psychiatry, with the exception of group therapy,[26] been developed by Europeans (Table 2)—and this in spite of the fact that the American Psychiatric Association has over 8000 members and that almost 5000 physicians have been certified by the American Board of Psychiatry and Neurology. In order to understand the disparity in original contributions between American and European psychiatrists, the difference which exists in the development of the basic sciences has to be mentioned.

Basic Scientists Are Scarce in America

The contributions of native Americans are not evenly distributed over all fields of human endeavor. In literature, music—and particularly jazz—and in motion pictures

TABLE 2.—*The Origin of Psychiatric Therapies*

Approximate Date	Place	Name	Therapy
1801	Paris	Pinel	Humane treatment of insane
1869	Berlin	Liebreich	Chloral hydrate introduced into medicine
1890	Paris and Nancy	Charcot and Bernheim	Hypnotherapy
1895	Vienna	Freud	Psychoanalysis
1903	Berlin	Fischer	Barbital (Veronal), the first barbiturate
1905	Boston	Pratt	Group therapy (class method)
1910	Frankfurt am Main	Ehrlich	Arsphenamine (Salvarsan)
1918	Vienna	Wagner von Jauregg	Malaria therapy
1920	Zurich	Klüst	Prolonged sleep
1931	London	Horsley	Narcoanalysis
1933	Vienna	Sakel	Insulin coma
1934	Budapest	Meduna	Pentylenetetrazol (Cardiazol) shock therapy
1935	Lisbon	Egas Moniz	Prefrontal lobotomy
1938	Rome	Cerletti and Bini	Electroshock therapy
1942	London	Fleming and Florey	Penicillin
1951	Paris	Rhone-Poulenc Laboratory	Chlorpromazine
1952	Basel	Ciba Laboratory	Rauwolfia

and theatrical productions, American writers, performers, and producers are known the world over. In engineering and in the applied sciences American achievements are well known. The same applies to certain sports; for example, in the track and field competition at the Olympic Games, 1952, the United States team won 16 out of 24 first places.[24] But the reverse seems to be true for contributions which fall within the realm of basic science, including the creation of new therapeutic methods. Mills, a sociologist, writes[38]: "The United States has never been a leader in basic research which it has imported from Europe. . . . Out of the $2 billion scientific budget of 1955, only $120 million (6 per cent) was for basic research. . . . There are only 10,000 engaged in fundamental research in all branches, and informed opinion has it that the top-rate creators number no more than one or two thousand."[38] Conant, former president of Harvard University, states[40]: "Until comparatively recently and except in a few outstanding cases, the United States has not led others in fundamental research." Vannevar Bush, wartime chief of the Office of Scientific Research and Development, writes[7]: "A nation which depends upon others for its new basic scientific knowledge will be slow in its industrial progress and weak in its competitive position in world trade, regardless of its mechanical skill."

The American weakness in basic science is reflected in the distribution of Nobel Prizes. Although no board of experts is infallible, the Nobel Prize committee seems to award this coveted honor in a fair and well-founded manner to those who have made fundamental contributions. From Table 3 it becomes clear that the United States falls well behind Europe in terms of total awards received.

TABLE 3.—*Nobel Laureates: 1901-1954*

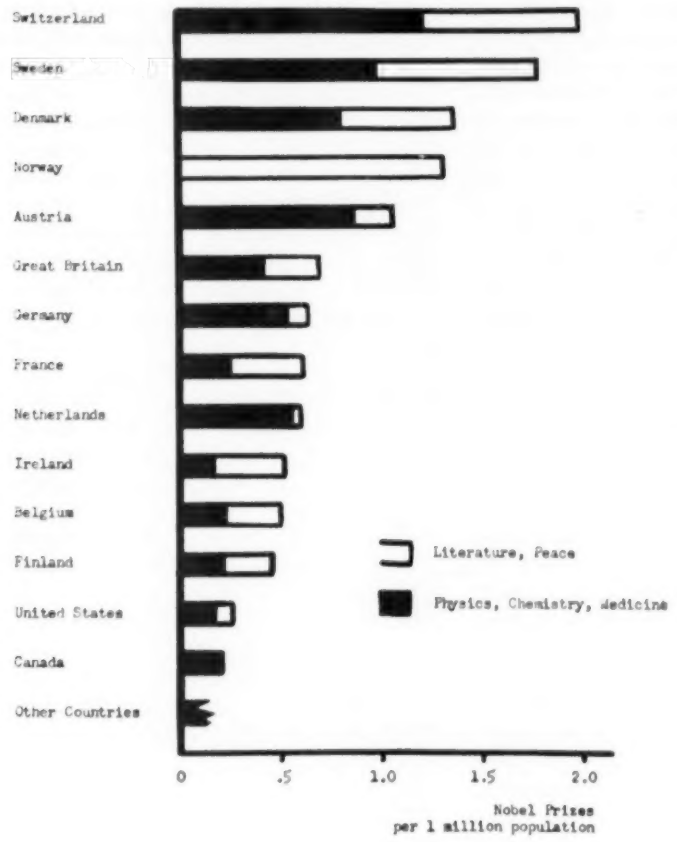
	Medicine	Other Disciplines
United States	11½	30
Western parts of Europe	29½	136½
Other countries	4½	9

Bureaucracy Stifles Originality and Interferes with Education

The appearance of original and fundamental contributions to science and culture seems to depend upon the size of the country. When Nobel Prizes are corrected for population, the smaller nations fare much better than the larger countries (Chart), which like the United States, suffer from the untoward effects of size upon social organization. The bigger the enterprise, the less can conditions be tailored to personal needs and the more do bureaucratic practices tend to submerge the individual. Large nations seem to lead in fields where achievement depends upon teamwork and the expenditure of money; small nations seem to lead in achievements which are germane to the originality and inventiveness of the individual.

Wherever there exists a powerful bureaucracy, the temptation to become a "figure" on the national or local scene is great. To hold office in an association; to organize research, education, or service on a large scale; to be a member of important committees; to be involved in consulting with state or federal agencies—these are the marks of successful professional. If a young man in an academic setting shows any promise, he soon is promoted into administrative positions. His time is more and more taken up with meetings and paper work and less and less with investigative pursuits or the practice of therapeutic skills.[20]

But why, we may ask, do intelligent people put up with this mass of red tape.[32] The answer is to be found in the fact that administrators and businessmen—and professionals who act like them—get top billing. Extension of spheres of influence is rewarded rather than penetrating exploration. In many of the smaller countries, in contrast, the individual is rewarded with prestige for mastery of a subject matter.[16] Here, the administrative load as the head of a national organization is not overwhelm-



Nobel Prizes by countries (1901-1954).

ing. Much paper work is obviated because details are handled by word of mouth. Top university positions, therefore, can still be held by the actual leaders in the field. Administrative duties do not take up all the energies of the professor, and his income equals that of other successful professionals in private practice, or exceeds it.

While in business and government it is feasible to have an administrator or executive in a top position, the application of big-business methods to science and art has had disastrous results upon education and the procurement of scientists. If the top-status carriers in a medical school—that is, presidents, deans, chairmen of departments, and professors—are not scientists, but merely professionals who got a degree and soon thereafter went into administration, the student cannot take these men as examples because they themselves have nothing to give. A student can learn only from a subject-matter-oriented teacher who has broad knowledge and skill; but if this teacher enjoys less recognition and status than the administrator whose skill is organizational and nonspecific for the subject matter, the student is faced with a conflict. Status-wise, he is attracted to imitate the administrator; content-wise, the subject-matter-oriented professional, in the lower echelons of the hierarchy. Just as the soldier's morale depends upon his relationship to his superiors, the young student's morale depends upon whom he can take as a model among his teachers without any

mental reservations. Combat soldiers do not identify with desk generals, nor do students identify with administrators. Faced with such a dilemma, the student then learns techniques from those in the lower echelons of the hierarchy and politics and business approaches from those higher in the hierarchy. But what he misses are the subtleties of thinking, reasoning, and decision making which, when combined with skill, characterize the creative and successful professional.

The Steelman report[51] on the nation's medical research emphasizes that "research is inseparable from the training of scientists. The stimulation of fundamental discoveries must be a keystone in the over-all expansion of medical research. The federal government must take the lead in this field by increasing promptly its support of basic research." But such support means not only to give money but to give money at the right place. If funds were to be placed in the hands of those who work as investigators and teachers rather than into the hands of those who run departments, hospitals, institutions, and associations, the bureaucratic atmosphere could be minimized. No medical, psychiatric, or scientific discovery has ever been made by a bureaucrat, nor has he ever advanced new theories or points of view. The clue to any advance is the individual, and without emphasis upon the individual no advance will be forthcoming. Perhaps the policy of fund-giving agencies should be changed from subsidy of research to subsidy of higher education. A man's character has to be molded in certain ways before he can absorb technical training without damage to his personality. And when he has become a specialist, he must work in a milieu that rewards skill and knowledge so that he can counteract the untoward effects of bureaucracy and technological specialization.

Sponsored Research May Result in Centralized Control

Fondness for organization and planning eventually leads to some kind of centralized control. The executive and consultative members of government agencies and private foundations form a sort of brain trust.[2] They are in constant touch with one another and hence share basic attitudes and beliefs. But, above all, the overlapping of memberships on various advisory boards nullifies the advantages of size the United States might otherwise possess, inasmuch as the various philosophical and theoretical principles upon which experimental or clinical procedures are based tend to be the ones that a few science-policy makers have agreed upon.[1] When the receipt of funds depends on good public relations, the workers tend to concentrate on sure bets—that is, the obvious.[15] When support hinges on being a member of the disbursing committee or on working in a large or famous university,[37] diversification is seriously handicapped. In psychiatric research, this is felt in the evolution of fashion trends: In the 1930's money was put into neurophysiological studies; in the '40's psychodynamic studies became the fashion; in the early '50's group studies moved into the foreground. Now the promising horse seems to be chemistry.[3]

In Europe, where most research funds form an integral part of the regular budget allocated to university departments and hospitals, centralized control is avoided altogether. Science-policy decisions and allocations of funds are made by the individual professor and chief. The political subdivision of the continent becomes an advantage. The northern, southern, and western parts of continental Europe and the United Kingdom, all of which lie west of the Iron Curtain, comprise some 17 independent nations (excluding the tiny principalities and republics), with a total of about 276,000,000 people. Each of these nations has separate universities, money sources, and governing agencies. No individual member who sits on an educational board has anything to say about what happens in any of the other countries; no science-policy decisions are made which affect the whole continent. Variety of policies,

differences in basic philosophies, and avoidance of overlapping directorates seem to have paid off in terms of the scientific, therapeutic, artistic, and humanistic achievements of these countries.[17] Avoidance of centralized control thus becomes for us a primary task.

Excellence is Penalized

In Europe, the quest for power and the striving for key positions in organizations are attenuated by the fact that power is compartmentalized. Each country has several parallel status hierarchies, such as the bar, the clergy, the military, the men of ideas (philosophers, writers, teachers, and scientists), the engineers, the artists, the civil servants, the craftsmen and artisans, the farmers, the industrial workers, and the businessmen. Each of these hierarchies has its own yardstick for measuring achievement and awarding status to meritorious members of the system. The businessman will be judged by the ethics that govern his transactions as well as the income he makes; the artisan will be judged by the quality of his product; the thinker by the originality of his theory, and the civil servant by his devotion to duty. In each occupation, a man's prestige is rated primarily by the excellence of his work, and only secondarily by criteria of practicality or the cash return.

Although in the United States there exist just as many different occupations as in Europe, we have only two status hierarchies —power and money—and one is translatable into the other. The result is that a district attorney can become governor, a general may be made the chairman of the board of an industrial corporation, and a businessman may serve as a regent of a university. The single prestige scale favors the development of jacks-of-all-trades and penalizes those who strive for excellence. The system is obviously a carry-over from the pioneer days, when a man had to be a builder, farmer, hunter, Indian fighter, and trader if he wished to survive. But with the disappearance of the frontier and the nomadic way of life, the overly versatile man is no longer needed and the professional or specialist comes into his own. But people in the United States look askance at persons whose skill and knowledge set them in a class by themselves. As long as success is defined in terms of money or power, theoretically, at least, everybody has an equal opportunity.[15] But excellence in skill and knowledge, particularly if it requires special education, for which not everybody is qualified, makes for inequality. In America it is considered bad taste to show one's competence, and people resent those who do things to perfection. This attitude may cost the United States its leading world position, which at present is based upon technological achievements. But since industrialization and technical know-how are quickly spreading around the globe, such skills soon will become commonplace. Under these changed conditions, a leadership position can be retained only by those who excel in originality of ideas, the quality of their products, and the expertness of their performance. In such a world, there will be little room for bungling amateurs. Writes Stuart Chase[19]: "Russia cannot match us in producing Chevrolets and IBM machines, at least not yet, but she proposes to beat us in producing *ideas* and *trained manpower*—a large part for export."

Commitment to a field of interest requires not only appropriate rewards but also a particular kind of life if the individual wishes to insure his continued growth.[8,9,22] But in adult life there are many forces which oppose the development of a way of living suitable for the investigator.[29] Foremost among them is the attitude of the public. In the light of American values, the physician who enters an academic career is often considered by others to be incapable of earning a living in private practice. The name of "egghead" spelled out by some politicians—perhaps with some justification—has hardly been used in a complimentary or affectionate way. The scientist is thus hemmed in by a double bind. If he excels, he is attacked for ivory

tower behavior; if he is average, he is discarded as unessential. The solution to the problem is to help the scientist accept his unloved position and to take as reward the somewhat distant respect of the population, which he will receive if he excels in integrity, higher morality, and creativity. But in order to achieve this goal, higher education is of the essence.

Democratic Education Should Not Require Elimination of the Fittest

Education toward excellence begins early. But few are the opportunities in our country for gifted children to enter schools where they meet talented peers who, like them, have been destined for professional careers. In our school system, which favors mass education and the ungifted child, the really talented child gets bored and does not receive proper attention.[4] How can any gifted child be challenged to do his best if, as reported in New York City, the students in academic high schools have an average I.Q. of 103, those in the vocational high schools an I.Q. of 85, and the so-called "displaced pupils" an I.Q. of 75 or lower?[6] Why should the average high school prepare the pupils for college if only 53% of those graduating in the highest fifth of their class go on to college?[18] Owing to the lack of discrimination between gifted and ungifted children, and to the lack of early preparation for a given career, the American child is for 20 years of his life exposed to an education that supposedly prepares him for everything; and, being pressurized to conform to an undifferentiated pattern, he soon loses what curiosity he may have had. The above-average child might be pulled up were there appropriate stimulation, whereas now he often is encouraged to coast along and make little effort. Apparently, businessmen and larger corporations are realizing this shortcoming and are beginning to introduce ways and means to educate an elite.[38] But the professions have done little, if anything, in this direction, while, according to Meyer,[34] epidemiologist, bacteriologist, and educator, the Russians apparently are "ruthless in eliminating the less gifted medical students from the higher echelons of the profession."

Robert M. Hutchins, former chancellor of the University of Chicago, puts the blame squarely on the universities.[25]

> We live in a world that is not merely unintellectual but anti-intellectual as well. Even the universities are anti-intellectual. The college, we say, is for social adaptation; the university is for vocational adjustment. Nowhere does insistence on intellectual problems as the only problems worthy of a university's consideration meet such opposition as in the universities themselves.

The result of such an attitude is that America is left without basic thinkers and scientists.

If the spread of the intelligence quotients of people who can perform work ranges from about 75 to over 150, it becomes quite clear that, in order to be democratic and to give everybody an equal opportunity, people have to be trained according to their abilities. Cox,[12] in his study of the life histories of 300 geniuses, points to the fact that the vast majority received special attention and education in their formative years. As a matter of fact, their whole way of life was subordinated to their career, particularly in the intellectual occupations. But even geniuses require an assortment of educational opportunities, as evidenced by the wide spread of their estimated I.Q.'s. Since measurement of intelligence favors the person who deals with words and numbers and penalizes the individual who engages in action, it is not surprising that philosophers and scientists have the highest I.Q.'s, writers, statesmen, and religious leaders are in the middle, and artists and soldiers range lower. While the American educational system has produced many leaders among soldiers, artists, statesmen, and writers, it has produced few in the categories of philosophers and basic scientists. Apparently our school system penalizes the very bright. But there really is no reason why this state of affairs should continue if proper high schools for the talented children were

organized and if the long summer vacations were cut in half. Interruption of instruction during the summer was appropriate in an agricultural economy, but when it comes to the training of professionals education has to continue throughout the year.

Furtherance of Psychiatric Research Depends upon an Emotionally and Intellectually Mature Elite

Intellectual growth and higher learning fall on barren soil if not accompanied by emotional maturity. This is particularly relevant for the psychiatric investigator.[28] While contributions in mathematics, physics, and chemistry tend to be made by scientists in the early years of their careers, contributions in the social sciences and medicine are usually made by people in their mature years.[30] Because of longer training in psychiatry, the age at which creative contributions are made may be set even higher. Freud was 44 when his book on dream interpretation was published. Bleuler was 54 when he published his work on the schizophrenias. The life histories of prominent psychiatrists and psychotherapists indicate that most of them had rather diversified life experiences, in terms of culture change, of personal experience with disease, or of changes in occupation or specialty.[42] All of these psychiatrists had enjoyed a higher education which required an attitude of curiosity, multiple identification, learnedness, skill, and questioning of what "authorities" said rather than a technological attitude of "how to do it." But in recent years, unfortunately, psychiatric and psychoanalytic education has become vocational training, on which subject Hutchins[25] aptly remarks: "We may get order in the higher learning by removing from it the elements which disorder it today, and these are vocationalism and unqualified empiricism."

Today in most psychiatric training centers, residents are not prepared for doing a pioneer job in the discovery of new principles and methods, but they are taught the techniques of psychotherapy, psychoanalysis, or shock therapy, as if these constituted the real answer to mental disease. This trend came into being during and after World War II, when the demand for psychiatrists and therapists was justified because they really were effective in alleviating the pressures of situational stress. But in peacetime the role of the psychiatrist changed. The initial hope that psychological treatment methods would change character and personality was not substantiated, and the field that was left to the psychiatrist was to ameliorate acute conditions and to help bring about emotional maturity and self-realization within the framework of the patient's character. But to accomplish this task, we do not need more and more psychiatrists who are trained less and less; we need an elite, highly educated and capable of preparing the younger generation for investigative work.

It takes mature people to help others to mature and to prevent narrow vocationalism. However, educational procedures have frequently run into a snag. The better and the longer an investigator is trained, the more he becomes conditioned to current views and teachings; consequently, he will be more liable to perpetuate the old and to be oblivious to the new. The newcomer and the unskilled researcher, in contrast, is likely to make many errors which training helps him to avoid. The traditional solution to this dilemma has been to advise young men not to remain too long in the same place or to study the same subject forever. Exposure to diversified methods, theories, and people not only forces a person to integrate but induces him later to tackle a problem from many angles. Narrow exposure, in contrast, contributes to making people technicians rather than thinkers. Unfortunately, today the three- or five-year residency training programs prevent young men from seeking education in various places at home and abroad.

Selection Eliminates Creative People

Another factor that operates toward uniformity in thinking and the elimination of

potentially creative people is the existence of rigid screening devices. If gravel is passed through progressively finer screens, the particles tend to become more uniform. The more applications for research are screened [15] and the more carefully personnel is selected, the greater are the chances of eliminating deviations. But all novelty is deviant when it first appears, and its creators frequently do not fit into the average mold. Screening, selection, and control thus are useful devices to perpetuate the old and to eliminate the new. Too long have we judged the scientists, intellectuals, and artists from the standpoint of whether they are capable of getting along in a group or whether they are free of character traits which are objectionable to the businessman, such as being superior, aloof, or dependent. For the selection of creative talent, there is but one method: self selection. People who are creative, regardless of their personality, will come forward eventually with their contributions if they are left in peace.

In many instances, academicians are screened with regard to criteria which do not apply to the function they are to perform. Demands for a cliché-type, all-round performance, which by necessity excludes the creative, may even be spelled out in the instructions to appointment and promotion committees. At the University of California, for example, university and public service is considered on a par with teaching, research, and professional competence.[56] But if the promotion of a scientist is dependent upon the number of speeches he has given to the public or the number of university committees he has been on, he is judged by negative criteria. Each hour spent in committee work and each day used to prepare a speech prevents the scientist from pursuing his investigations. These official instructions in effect amount to an implicit recommendation to promote a faculty member if he neglects his scientific work. In a good many American medical schools, a professor may spend more than half his time—and a department chairman or a dean close to three-fourths of his time—in conference work, not to mention the time spent in signing requisitions, absence reports, and so on. Ultimately such a person becomes very prominent, usually at the price of being completely ensnared in red tape and becoming creatively sterile.

Arranging get-togethers, raising money, giving speeches to lay groups, presiding over committees, going to meetings, holding offices in organizations—all these are activities which suit the extrovert. Most administrators, having chosen action and human organization as their field, are outgoing people. Their concept of the successful man is an adaptable, action-oriented, somewhat unimaginative person. The great advances in science, mathematics, and philosophy, however, have been made by introverts—a type that usually is eliminated by the administrator as being too impractical. Perhaps one could think of the administrator as a person whose task it is to put up with the deviant features of talented people and to facilitate their work rather than to select those who make his life easy—the conformists and uncreative people.[43] As long as the introverted personality type does not find a respected place on the American scene and does not receive the opportunity to shape his life in his own way without being penalized, basic contributions are not going to rise much above the level of platitudes.

Summary and Specific Recommendations

A nation like the United States cannot maintain its leadership position by relying upon import of original ideas and neglecting the development of basic sciences.

The furtherance of people who have original ideas and are capable of creative contributions hinges upon the presence of an intellectual milieu and appropriate recognition of the contributions that introverted people have made. At present, the educational system from grade school to university is geared to produce outgoing, action-oriented people.

The preparation for a scientific career has to start early. It has to be based on

character and scientific education of about equally talented youngsters. For this purpose, the educational system has to provide for two types of schools: average schools for the average pupil; special schools for the gifted child. At the high school level, the college preparatory institution should be separated from the professional school preparatory institution. The schools should be open to poor and rich alike, and admission should be based on talent and achievement.

The training of psychiatrists has to be based upon a broad higher education rather than on narrow vocationalism. Loyalty to truth, novelty, progress, knowledge, and skill, which are the earmarks of the professional, should replace loyalty to income, security, status, and know-how, which are the trademarks of the businessman and technician.

The compensation of university professors, research workers, and teachers has been so reduced in the last 50 years that salaries have to be tripled in order to restore the relative position of the academician in the community as it existed at the beginning of this century.

Science-policy decisions should be decentralized. Membership on more than one disbursing committee should not be encouraged, and acceptance of funds by members of the committee should be considered undesirable. Money appropriated for research should be divided into small sums and distributed among many persons throughout the nation. This procedure minimizes bureaucratic red tape and centralized control.

At present, research which is basic to psychiatry is essentially theoretical. The most urgent requirement is the development of a unified theory of human behavior so that physical, psychological, and social approaches to man can be expressed within one system.

A careful review of the assumptions underlying psychiatric progress and the notions of health and disease is needed in order to decide whether the procedures used in natural science—reductionism, analysis, and concern with mass effects—are useful in the study of abnormal human experience.

Pending the settlement of such basic questions, multiple programs of inquiry—based on a variety of assumptions—are indicated. Not knowing in which direction psychiatry is going to develop, its research has to be put on the broadest possible basis. Project and developmental research, being technological in nature, should at the present be curtailed in favor of theoretical research and true exploration of the unknown.

Langley Porter Clinic, Parnassus at First Ave.

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Frontal Lobe Damage and Flicker Fusion Frequency

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Flicker fusion frequency is the number of light-dark cycles per second at which an intermittent light is perceived by a particular subject as a steady point of light without semblance of flicker. Investigations of this phenomenon have indicated a linkage between it and various physiological and psychological characteristics.* Two studies in particular have raised the possibility that frontal lobe damage may be reflected in a depressed fusion point or in the variability displayed in fixing the point of fusion.†

The present study was designed to assess the long-range or permanent effects of bilateral prefrontal lobotomy on flicker fusion frequency when adequate control groups are employed.

Procedure

A total of 116 subjects were involved in the investigation. Three matched groups were directly concerned with the effects of frontal lobe damage on the fusion point:

1. A group of 26 patients lobotomized 8.6 years prior to testing.
2. A group of 18 control patients hospitalized over the same period of time but not subject to surgery, largely because of relatives' objections. The groups were equated for race, sex, age, institutionalization period, formal schooling, and diagnosis.
3. A group of 50 normal subjects comparable in race, age, sex, and educational background to the previous two groups. These were persons who were functioning effectively in their respective jobs and social settings and had no history of psychiatric disorders, neurological disease, uncorrected visual anomalies, or periods of unconsciousness as a result of head injuries.

In addition to these three groups, a group of 22 young normal subjects was included as a downward extension in age of the regular normal group. These subjects were included for the information that could be gained about the effect of age on fusion frequency, not for comparison with the surgical and nonsurgical groups.

The accompanying Table indicates the close similarity of the three matched groups and the salient features of the young normal group.

The apparatus for determining flicker fusion frequency consisted of a motor-driven rotator device utilizing a light of moderate brightness and a fixed light-dark ratio of 12.5:87.5.

Each subject was given three practice exposures to the flickering light, moving from obvious flicker to the point of perceived fusion and then well beyond. Five determinations of fusion point were recorded for each subject. The mean or average denoted the flicker fusion frequency for that particular person.

Results

Comparison of the mean fusion point for each of the three matched groups showed no statistically significant differences. Fusion frequency, in cycles per second, for each of the groups was as follows: operatees, 37.1; hospitalized controls, 38.3; normal controls, 36.9.

As would be expected, the young normal group (mean age 21.3 years) showed a significantly higher fusion point (41.6 cps) than the older normal control group. The difference was significant well beyond the 1% level of probability and indicates that the apparatus employed was sufficiently sensitive to pick up differences between surgical and nonsurgical groups if any existed.

Plotting the mean fusion point for each 10-year grouping of the combined normal groups from 18 to 75 years of age showed a definite gradual decrease in fusion level with advancing age. The point of greatest decrease seems to occur between 45 and 55

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† References 1-2.

Control Features for Groups Employed in Flicker Fusion Determination

Group	No.	Age, Yr.		Years Institutionalized		Years of School	Diagnosis	
		Mean	Range	Mean	Range	Mean	Schizophrenic	Manic-Depressive
Operatees	26	52.5	34-69	22.9	12-42	9.2	19	7
Controls	18	52.7	30-74	21.6	11-37	8.7	13	5
Normals	50	52.6	30-75	--	--	9.6	--	--
Young normals	22	21.3	18-29	--	--	14.0	--	--

years of age. This negative linear relationship between fusion frequency and age was apparent in the two hospital groups as well ($r = -0.43$, significant well beyond the 1% level of probability).

Intraindividual variability, the extent to which a subject varies about his own mean, and expressed by the average deviation, was not significantly different for operatees and controls. Actually, both the hospitalized groups showed a slightly greater variability than either of the normal groups.

Apparently the incidental damage to the frontal cortex and the more extensive damage to the subcortical structures resulting from bilateral prefrontal lobotomy do not produce either a permanent depression of fusion point or a decreased variability (greater accuracy) in locating that point. Damage to areas of the brain other than the frontal lobes may well be reflected in alterations of flicker fusion frequency, but the kind and extent of damage resulting from prefrontal lobotomy are not so reflected.

Other effects of age on flicker fusion frequency were apparent from analysis of the total normal group (72 subjects):

1. Interindividual variability, as measured by the standard deviation of the age groups, decreases markedly with age. The range of fusion scores in the oldest groups is less than half that in the youngest group.
2. Low or minimum fusion frequencies are present in the youngest, as well as in the older, groups.
3. The extent to which an individual subject varies or deviates from his own mean fusion point in successive trials does not appear to be influenced by age. There is no evidence that older subjects are less variable (more accurate) than young subjects.

Summary

Matched groups of patients who had sustained bilateral prefrontal lobotomy, hospitalized control patients (nonsurgical), and normal control subjects were tested for flicker fusion frequency. Surgery for the operatee group had been performed from eight to nine years prior to testing. Pertinent control criteria were race, age, sex, period of time institutionalized, amount of schooling, and preoperative diagnosis. The findings of the study are as follows:

1. The frontal lobe damage sustained in prefrontal lobotomy is not reflected in a permanently depressed fusion point.

2. There is no indication that lobotomized subjects are objectively more accurate (less variable) in locating their fusion point than are hospitalized control or normal control subjects.

3. A definite linear decrease in fusion frequency level with age is found in patient and in normal subjects.

4. The most pronounced drop in fusion level with age occurs between 45 and 55 years of age.

5. The extent to which a subject varies or deviates from his own fusion point in successive trials does not appear to be dependent on age. There is nothing to indicate that older persons are less variable than young persons.

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Books

BOOKS RECEIVED

We acknowledge receipt of the following books. Only those books will be reviewed which the Editorial Board finds suitable for this journal.

On the Early Development of Mind. By Edward Glover. Price, $7.50. Pp. 483. International Universities Press, Inc., 227 W. 13th St., New York 11, 1956.

Management of Emotional Problems in Medical Practice. Edited by Samuel Liebman, M.D. Price, $5.00. Pp. 152. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5, 1956.

Psychiatric Research Reports of the American Psychiatric Association: 5. Research Techniques in Schizophrenia. Edited by members of the Committee on Research, 1955-1956. Price, $2.00. Pp. 153. American Psychiatric Association, 1785 Massachusetts Ave., N. W., Washington 6, D. C., 1956.

Taboo. By Franz Steiner. Price, $4.75. Pp. 154. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1956.

Mind Over Matter and Matter Over Mind. By Giuseppe Tortorici. Price not given. Pp. 24. The William-Frederick Press, 313 W. 35th St., New York 1, 1956.

The Facts of Mental Health and Illness. By K. R. Stallworthy. Price not given. Pp. 215. N. M. Peryer Limited, 145-147 Worcester St., Christchurch, C. 1., New Zealand, 1956.

Psychiatry: the Press and the Public. Edited by Wilfred Bloomberg and others. Price, $1.00. Pp. 80. American Psychiatric Association, 1785 Massachusetts Ave., N. W., Washington, D. C., 1956.

Psychology, Psychiatry, and the Public Interest. Edited by Maurice H. Krout, Ph.D. Price, $4.00. Pp. 217. University of Minnesota Press, Minneapolis 14, 1956.

Dynamic Psychiatry in Simple Terms. By Robert R. Mezer, M.D. Price, $2.50. Pp. 174. Springer Publishing Company, Inc., 44 E. 23d St., New York 10, 1956.

Encyclopedia of Morals. Edited by Vergilius Ferm. Price, $10.00. Pp. 682. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1956.

Speech Disorders: Principles and Practices of Therapy. By Mildred Freburg Berry and Jon Eisenson. Price, $6.75. Pp. 573. Appleton-Century-Crofts, Inc., 35 W. 32d St., New York 1, 1956.

Basic Readings on the MMPI in Psychology and Medicine. Edited by George Schlager Welsh and W. Grant Dahlstrom. Price, $8.75. Pp. 656. University of Minnesota Press, Minneapolis 14, 1956.

Group Processes: Transactions of the Second Conference, Oct. 9-12, 1955. Edited by Bertram Schaffner, M.D. Price, $3.50. Pp. 255. Josiah Macy, Jr. Foundation Publications, 16 W. 46th St., New York 36, 1956.

BOOK REVIEWS

Anxiety and Magic Thinking. By Charles Odier, M.D.; translated by Marie-Louise Schoelly, M.D., and Mary Jane Sherfey, M.D. Price, $5.00. Pp. 302. International Universities Press, 227 W. 13th St., New York 11, 1956.

This book is a translation from the French of a study which the translators contend bridges a gap between the psychoanalytic and the Piaget school of psychology. The

translators state that Odier's style was so highly individualistic that their task was very difficult. Perhaps they have done a very good job, but the American psychiatrist will have difficulty in reading the English translation. The style is still highly personalized, the vocabulary not that of psychoanalysis but a combination of Odier and Piaget. There is a host of breezily made statements of fact without logical determination or empirical data. The experienced reader will be stimulated to disagreement with every chapter. Perhaps for those who are familiar with Piaget's special terminology, less difficulty will be encountered. At any rate, the book is worth a try at reading by dynamic psychiatrists. There is no bibliography and no index.

Research Techniques in Schizophrenia. Psychiatric Research Reports No. 5 of the American Psychiatric Association. Editor, Jacques S. Gottlieb, M.D. Price, $2.00. Pp. 153. New York, 1956.

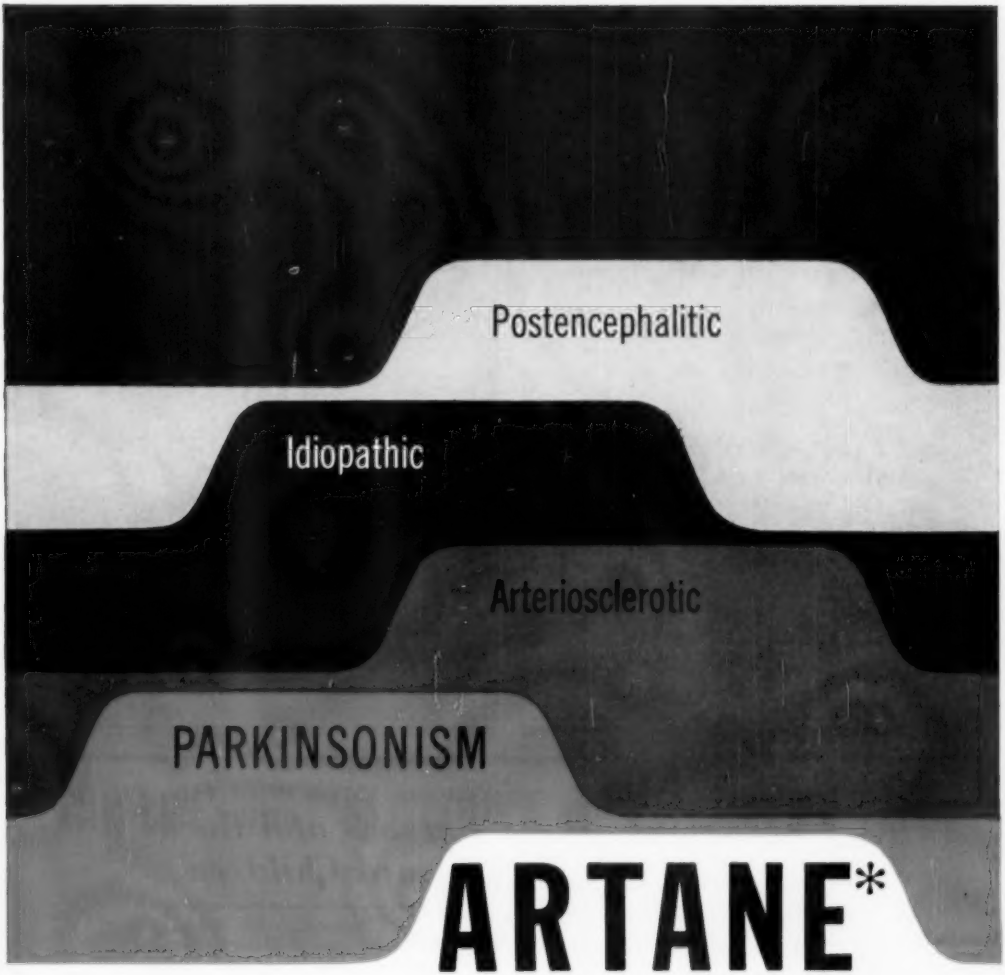
In this paper-bound volume concerned with research techniques in schizophrenia, five presentations are made, followed by active discussion by members of a special board of discussants. Both the prime presentations and the discussions are well edited and easily understandable.

John Lilly relates his work on the mental effects of reduction of ordinary levels of physical stimuli on intact healthy persons. This symposium is fascinating for its material concerned with psychodynamics and neurophysiology. If only for this symposium itself, the book is worth while.

Jerome K. Myers reports on the Yale studies of social and psychological variables in relation to schizophrenia. Morton Kramer and his group present the application of life tables to the study of mental hospital populations. Barbara Betz and John Whitehorn summarize their studies of the relationship of the therapist to the outcome of therapy in schizophrenia, which was a very illuminating research.

Finally, Ogden Lindsley discusses operant conditioning methods applied to research in clinical schizophrenia, which is the application of Skinner's techniques to human subjects. The last symposium brought up quite a vigorous critical discussion by Kline and others.

This small volume is extremely interesting and valuable for an orientation regarding some research in schizophrenia. It may be procured from the American Psychiatric Association, 1785 Massachusetts Ave., N.W., Washington 6, D. C.



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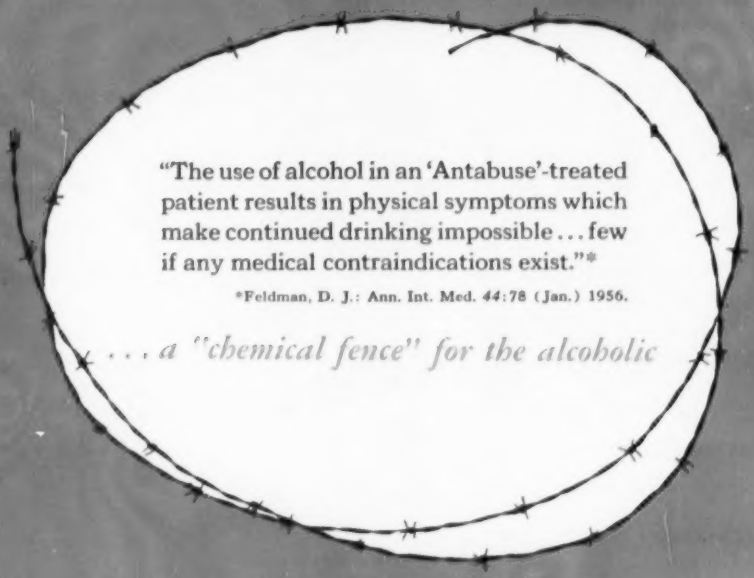
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1. Freed, H., and Peifer, C.A.: Am. J. Psychiat. *113*:22 (July) 1956.

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